Appendix B

Air Quality Study

Giroux & Associates
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AIR QUALITY IMPACT ANALYSIS

REYNOLDS RANCH

CITY OF LODI, CALIFORNIA

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METEOROLOGY CLIMATE

The climate of San Joaquin County, as with all of California, is dominated by the strength and position of semi-permanent high-pressure cell over the Pacific Ocean north of Hawaii. In summer, when the high is strongest and farthest north, temperatures are hot and humidity's are low, but persistent afternoon and evening breezes somewhat help to moderate the summer heat. In winter, when the high is weakest and farthest south, weather patterns are more changeable as occasional storms are interspersed with protracted periods of stagnant, fair weather conditions.

Temperatures at the project site average 59°F annually with a moderate to strong seasonal oscillation. Summer afternoon's average in the low 90's while winter nights are generally in the upper 30s. Although maxima of 108 degrees and minima down to 21 degrees have been observed in Lodi, extremes of temperature are somewhat moderated by the proximity of the Pacific Ocean. About 70 days per year exceed 90 degrees, while about 35 days drop to just below freezing.

The annual rainfall as measured in Lodi, which falls almost exclusively from late October to early May, totals 16.3 inches per year, but varies significantly from year to year. Measurable rain falls on about 34 days per year but only 11 of those days have moderate rainfall of more than 0.5 inches in 24 hours.

Winds across San Joaquin County show a number of distinct patterns depending on the driving mechanism and the topographical steering of both the Delta and the Central Valley axis. The dominant winds across Lodi are from west to east from the strong marine air infow from the cool Bay Area to the warm Central Valley. They turn toward the southeast across Lodi as they head up the San Joaquin Valley. Winds are dominantly from the W-NW, except during occasional periods of poorly disorganized valley winds when the cross-valley component is dominant. During summer, the onshore flow from ocean to land creates a strong inflow into the San Joaquin River Valley that may bring air pollution into San Joaquin County from the Bay Area. During winter storms, the Valley topography also funnels the winds with a dominant and well-organized flow again from the NW. Between the winter storms, winds are often light with weak downvalley flow from the east or southeast toward the Delta.

The net effect of the observed wind patterns is that daytime mixing in the project area, especially in summer, is generally good. Any observed air pollution effects of local emissions sources tend to occur many miles away from the source in response to prevailing wind patterns. At night, especially in winter, the near calm winds tend to localize the impact from any emissions sources. Winter air quality patterns tend therefore to be dominated by micro-scale dispersion processes with generally good air quality except in very close proximity to freeways, parking lots or highly congested intersections. In the absence of any significant development in the Lodi area, the limited dispersion potential from the weak nocturnal winds is probably not a significant air quality issue except for possible agricultural activity emissions stagnation.

In addition to prevailing wind patterns that control the rate of dispersal and trajectory of local pollutant emissions, the San Joaquin Valley Air Basin (SJVAB) experiences two types of

inversions that affect the vertical depth through which pollutants can be mixed. In summer, air within the high pressure cell over the region warms by compression as it sinks. The resulting warm layer aloft creates a lid over the region until surface heating late in the day finally destroys this subsidence inversion. These inversions contribute to summer photochemical smog problems by confining pollution to a shallow layer between ground surface and the inversion base aloft.

At night, especially in winter, the air near the ground cools by radiative processes, while the air aloft remains warm. Surface-based radiation inversions are formed that, in conjunction with nearly calm winds, cause localized air pollution "hot spots" to be created near emissions sources because of the very poor winter nocturnal dispersive capacity. These inversions burn off after sunrise, but are a factor in contributing to elevated nocturnal primary (unreacted) automotive air pollution levels such as carbon monoxide (CO). While the subsidence and radiation inversions are present throughout much of the year, they are much less dominant than on summer afternoons and winter nights, respectively. Their decreased importance during the spring and fall transitional periods leads to generally good air quality during these seasons.

AIR QUALITY SETTING

AMBIENT AIR QUALITY STANDARDS (AAQS)

In order to gauge the significance of the air quality impacts of the proposed Reynolds Ranch project, those impacts, together with existing background air quality levels, must be compared to the applicable ambient air quality standards. These standards are the levels of air quality considered safe, with an adequate margin of safety, to protect the public health and welfare. They are designed to protect those people most susceptible to further respiratory distress such as asthmatics, the elderly, very young children, people already weakened by other disease or illness, and persons engaged in strenuous work or exercise, called "sensitive receptors." Healthy adults can tolerate occasional exposure to air pollutant concentrations considerably above these minimum standards before adverse effects are observed. Research suggests, however, that long-term exposure to air pollution at or above standards may lead to chronic adverse health effects. Just meeting standards may not provide a sufficient health protection cushion for sensitive receptor populations.

National AAQS were established in 1971 for six pollution species with states retaining the option to add other pollutants, require more stringent compliance, or to include different exposure periods. Because California had established AAQS several years before the federal action and because of unique air quality problems introduced by the restrictive dispersion meteorology, there is considerable difference between state and national clean air standards. Those standards currently in effect in California are shown in Table 1. A description of source and effects of those air pollutants with clean air standards is shown in Table 2.

Table 1 includes those federal clean air standards that were adopted in 1997. These standards included a chronic (8-hour) exposure limit for ozone and a standard for ultra-small diameter particulate matter of 2.5 microns of less (called PM-2.5). EPA's authority to promulgate clean air standards without a specific congressional mandate, and without a comparison of costs to air

quality benefits, was challenged in a series of court cases that culminated in the U.S. Supreme Court agreeing to hear the appeal in November, 2000. On February 27, 2001, the U.S. Supreme Court, in a unanimous decision, overturned the previously issued stay of implementation of the federal standards for ozone (8 hours) and ultra-fine particulate matter (PM-2.5). The Court ruled that EPA did not require specific congressional authorization for this action, nor did it have to consider the cost-benefit ratio of the action. However, the Court did find that the proposed implementation schedule for these standards was inconsistent. That inconsistency has since been resolved.

In addition to a variety of pollutants with ambient air quality standards (called "criteria pollutants"), air quality considerations may include pollutants which have no safe level of exposure (toxic or hazardous air contaminants), "normal" air constituents present in variable quantities (carbon dioxide, methane, water vapor), precursors to the pollutants (ammonia, chloride, sulfates, nitrates, etc, which form particulate matter), and nuisance pollutants such as odors or large dust particles that soil property.

The San Joaquin Valley Air Pollution Control District (SJVAPCD) has jurisdiction over air quality matters in the SJVAB. The SJVAPCD was formed in 1991. The air district is responsible for air quality programs in San Joaquin, Stanislaus, Merced, Madera, Fresno, Kings, Tulare and a portion of Kern County. The SJVAPCD has a large number of air quality responsibilities. For many years its primary role was in the control of stationary sources of air pollution. More recent legislation at the state and federal levels increased local air district responsibilities to implement transportation control measures (TCM's). The SJVAPCD also coordinates its air quality planning and improvement efforts with various councils/associations of governments, transportation planning agencies, as well as with economic development or trade associations to maximize the benefit and minimize the impact of air pollution improvement efforts.

The San Joaquin Valley has been designated as a non-attainment air basin by the EPA and the California Air Resources Board (ARB) for ozone and fine particulate matter. In response to state and federal clean air legislation the SVJAPCD is required to prepare and adopt air quality attainment plans on a prescribed schedule. The attainment planning process has generated multiple state-mandated plans, four federal ozone plans, three federal PM-10 plans and one federal CO plan since 1991.

The most significant and controversial air quality planning issue has focused on the 1-hour ozone standard. It become obvious several years ago that the basin could not demonstrate an adequate rate-of-progress to meet the 1-hour standard within the timetable required for a "severe" non-attainment area. A downgrade to an "extreme" non-attainment area was requested and granted that shifts the attainment deadline to 2010. The plan was locally approved and forwarded to the EPA in November 2004. This plan is the currently adopted blueprint for improved ozone air quality in the basin.

Table 1
Ambient Air Quality Standards

Pollutant	Averaging Time	California Standards		Federal Standards		
		Concentration	Method	Primary	Secondary	Method
Ozone (O_3)	1 Hour	0.09 ppm (180 µg/m³)	Ultraviolet Photometry	0.12 ppm (235 µg/m³)	Same as Primary Standard	Ultraviolet Photometry
	8 Hour	0.07 ppm (140 µg/m³)		0.08 ppm (157 µg/m³)		
Respirable Particulate Matter (PM_{10})	24 Hour	50 µg/m³	Gravimetric or Beta Attenuation	150 µg/m³	Same as Primary Standard	Inertial Separation and Gravimetric Analysis
	Annual Arithmetic Mean	20 µg/m³		50 µg/m³		
Fine Particulate Matter ($PM_{2.5}$)	24 Hour	No Separate State Standard		65 µg/m³	Same as Primary Standard	Inertial Separation and Gravimetic Analysis
	Annual Arithmetic Mean	12 µg/m³	Gravimetric or Beta Attenuation	15 µg/m³		
Carbon Monoxide (CO)	8 Hour	9.0 ppm (10 mg/m³)	Non-Dispersive Infrared Photometry (NDIR)	9 ppm (10 mg/m³)	None	Non-Dispersive Infrared Photometry (NDIR)
	1 Hour	20 ppm (23 mg/m³)		35 ppm (40 mg/m³)		
	8 Hour (Lake Tahoe)	6 ppm (7 mg/m³)		–	–	–
Nitrogen Dioxide (NO_2)	Annual Arithmetic Mean	(new standard pending)	Gas Phase Chemiluminescence	0.053 ppm (100 µg/m³)	Same as Primary Standard	Gas Phase Chemiluminescence
	1 Hour	0.25 ppm (470 µg/m³)		–		
Lead	30-Day average	1.5 µg/m³	Atomic Absorption	–	–	–
	Calendar Quarter	–		1.5 µg/m³	Same as Primary Standard	High Volume Sampler and Atomic Absorption
Sulfur Dioxide (SO_2)	Annual Arithmetic Mean	–	Ultraviolet Fluorescence	0.030 ppm (80 µg/m³)	–	Spectrophotometry (Pararosaniline Method)
	24 Hour	0.04 ppm (105 µg/m³)		0.14 ppm (365 µg/m³)	–	
	3 Hour	–		–	0.5 ppm (1,300 µg/m³)	
	1 Hour	0.25 ppm (655 µg/m³)		–	–	
Visibility Reducing Particles	8 Hour	Extinction coefficient of 0.23 per kilometer–visibility of 10 miles or more (0.07–30 miles or more for Lake Tahoe) due to particles when relative humidity is less than 70 percent. Method: Beta Attenuation and Transmittance through Filter Tape.		No Federal Standards		
Sulfates	24 Hour	25 µg/m³	Ion Chromatography			
Hydrogen Sulfide	1 Hour	0.03 ppm (42 µg/m³)	Ultraviolet Fluorescence			
Vinyl Chloride	24 Hour	0.01 ppm (26 µg/m³)	Gas Chromatography			

Table 2

Health Effects of Major Criteria Pollutants

Pollutants	Sources	Primary Effects
Carbon Monoxide (CO)	• Incomplete combustion of fuels and other carbon-containing substances, such as motor exhaust. • Natural events, such as decomposition of organic matter.	• Reduced tolerance for exercise. • Impairment of mental function. • Impairment of fetal development. • Death at high levels of exposure. • Aggravation of some heart diseases (angina).
Nitrogen Dioxide (NO_2)	• Motor vehicle exhaust. • High temperature stationary combustion. • Atmospheric reactions.	• Aggravation of respiratory illness. • Reduced visibility. • Reduced plant growth. • Formation of acid rain.
Ozone (O_3)	• Atmospheric reaction of organic gases with nitrogen oxides in sunlight.	• Aggravation of respiratory and cardiovascular diseases. • Irritation of eyes. • Impairment of cardiopulmonary function. • Plant leaf injury.
Lead (Pb)	• Contaminated soil.	• Impairment of blood function and nerve construction. • Behavioral and hearing problems in children.
Fine Particulate Matter (PM-10)	• Stationary combustion of solid fuels. • Construction activities. • Industrial processes. • Atmospheric chemical reactions.	• Reduced lung function. • Aggravation of the effects of gaseous pollutants. • Aggravation of respiratory and cardio respiratory diseases. • Increased cough and chest discomfort. • Soiling. • Reduced visibility.
Fine Particulate Matter (PM-2.5)	• Fuel combustion in motor vehicles, equipment, and industrial sources. • Residential and agricultural burning. • Industrial processes. • Also, formed from photochemical reactions of other pollutants, including NOx, sulfur oxides, and organics.	• Increases respiratory disease. • Lung damage. • Cancer and premature death. • Reduces visibility and results in surface soiling.
Sulfur Dioxide (SO_2)	• Combustion of sulfur-containing fossil fuels. • Smelting of sulfur-bearing metal ores. • Industrial processes.	• Aggravation of respiratory diseases (asthma, emphysema). • Reduced lung function. • Irritation of eyes. • Reduced visibility. • Plant injury. • Deterioration of metals, textiles, leather, finishes, coatings, etc.

Source: California Air Resources Board, 2002.

The 1-hour federal standard was replaced by an 8-hour standard in mid-2005. The deadline for approving a revised plan for the 8-hour ozone standard is 2007, and the attainment deadline for the basin is 2013. The 1-hour plan will continue to function as the operative attainment strategy until the 8-hour standard attainment plan replaces the current extreme non-attainment plan.

The California Air Resources Board (ARB) is required to periodically review the most recent health effects studies, and revise state AAQS accordingly. Based upon this mandate, the ARB has adopted, or is adopting, state standards for ozone (8-hour), PM-10, PM-2.5 and nitrogen dioxide (NO2) that are more stringent than their federal counter-parts.

BASELINE AIR QUALITY

San Joaquin Valley air quality primarily results from a combination or stagnant atmospheric ventilation, intense sunshine to drive photochemical reactions, and continuing growth/ urbanization. While agricultural activities continue to contribute to particulate emissions, much of the summer haze is due to ozone (smog). Motor vehicles generate 57 percent of smog precursors, with off-road vehicles, consumer products and small utility equipment adding 20 percent (www. Valleyair.org/newsed/apvalley.htm). The contribution of pollutants from outside the air basin is most pronounced near the gap in the Coast Range in the San Joaquin/Sacramento Delta. With continuing emissions improvements in the Bay Area, the smog transport problem into San Joaquin County is much less severe than what it was 10-20 years ago.

The combination of limited dispersive capacity and growth contribute to the continuing non-attainment status of the basin for several pollutants. Ozone and small-diameter particulates exceed standards by a substantial margin. While the South Coast (Los Angeles) Air Basin (SCAB) continues to have the poorest air quality in California, the gap between the San Joaquin Valley Air Basin (SJVAB) and the SCAB has been steadily narrowing. Whereas improvement over the last two decades has been pronounced in the SCAB, it has been only minimal in the Valley. Smog levels are almost identical downwind of Fresno or Bakersfield as they are in much of Los Angeles County.

Existing levels of ambient air quality and historical trends and projections in the project area are well documented from measurements made by the SJVAPCD in several locations in San Joaquin County. The most complete air monitoring measurements closest to the project site are made in Stockton. From these data one can infer that baseline air quality levels near the project site are occasionally unhealthful, but that such violations of clean air standards usually affect only those people most sensitive to air pollution exposure. Table 3 summarizes the monitoring history from the Stockton monitoring station for the last 5 years.

As reflected in the data in Table 3, the standards for ozone and for particulate matter (PM-10) are routinely exceeded near the project site, as they are throughout the air basin. The SJVAB is designated as a "non-attainment" air basin by state and federal agencies as shown in Table 4.

Table 3
Air Quality Monitoring Summary
(Days Standards Were Exceeded and Maximum Observed Concentrations)

Pollutant/Standard	2000	2001	2002	2003	2004
Ozone					
1-hour > 0.09 ppm (S)	4	5	2	3	1
1-hour > 0.12 ppm (F)	0	0	0	0	0
8-hour > 0.09 ppm	0	1	0	1	0
Max 1-hour Conc. (ppm)	0.107	0.103	0.102	0.104	0.096
Carbon Monoxide					
1-hour > 20. ppm (S)	0	0	0	0	0
8- Hour > 9. ppm (S,F)	0	0	0	0	0
Max 1-hour Conc. (ppm)	6.5	8.4	6.0	5.8	3.7
Max 8-hour Conc. (ppm)	3.9	6.0	3.2	3.1	2.5
Nitrogen Dioxide					
1-hour > 0.25 ppm (S)	0	0	0	0	0
Max 1-hour Conc. (ppm)	0.099	0.084	0.076	0.088	0.079
Respirable Particulates (PM-10)					
24-Hour > 50 $\mu g/m^3$ (S)	9/61	11/63	10/64	3/62	3/61
24-Hour > 150 $\mu g/m^3$ (F)	0/61	0/63	0/64	0/62	0/61
Max. 24-Hr. Conc. ($\mu g/m^3$)	97.	147.	91.	90.	61.
Ultra-Fine Particulates (PM-2.5)					
24-Hour > 65 $\mu g/m^3$ (F)	1/123	2/123	0/124	0/123	0/122
Max. 24-Hour Conc. ($\mu g/m^3$)	78.	76.	64.	45.	41.

(S) - State ambient standard; (F) - Federal ambient standard

Data from Stockton (Hazelton) Air Monitoring Summary,
Source: California Air Resources Board, PTSD-06-021-CD, 2006

Table 4

San Joaquin Valley Air Basin Attainment Status

Pollutant	Designation/Classification	
	Federal Standards	**State Standards**
Ozone – 1 Hour	Non-attainment/Extreme	Non-attainment/Severe
Ozone – 8 Hour	Non-attainment/Serious	No State Standard*
PM-10 – 24 Hour	Non-attainment/Serious	Non-attainment
PM 2.5 – 24 Hour	Unclassified**	No State Standard
Carbon Monoxide	Attainment	Attainment
Nitrogen Dioxide	Attainment	Attainment
Sulfur Dioxide	Attainment	Attainment
Lead Particulates	No Designation	Attainment
Other Pollutants (H2S, SO4, visibility)	No Federal Standards	Attainment or Unclassified

* State standard goes into effect in 2006, basin will be non-attainment.
** To be determined, but likely non-attainment.

However, Stockton (and, by inference Lodi) has not recorded any violations of the federal one-hour ozone standard in the last five years. The federal 8-hour ozone standard was exceeded only twice in five years. No more than three violations of federal standards in three years is considered as "attainment" under federal guidelines. Although the air basin as a whole is considered in "serious non-attainment" for the 8-hour ozone standard, the project area has considerably better ozone air quality than the rest of the air basin.

Table 3 includes data for PM-2.5. PM-2.5 monitoring was begun in 1999 following adoption of a federal standard in 1997. Based upon available PM-2.5 measurements the basin will be designated as "non-attainment" for the federal annual and 24-hour standards. PM-2.5 is different from more ordinary "dust" in that very little of PM-2.5 is created by the mechanical breakdown of larger particles. PM-2.5 is created mainly as a combustion byproduct (soot), or from chemical growth of microscopic materials. Health effects from elevated PM-2.5 exposure are believed to be more severe than from PM-10. Table 3 shows that although San Joaquin County experiences frequent violations of PM-10 standards from agricultural activities, very few violations of the PM-2.5 standard have been observed in the last five years because agricultural dust does not break down readily into PM-2.5.

More localized pollutants such as carbon monoxide, nitrogen oxides, etc. are low near the project site because background levels, never exceed allowable levels. There is substantial excess dispersive capacity to accommodate localized vehicular air pollutants such as NOx or CO without any threat of violating applicable regulations.

SJVAPCD Regulations

The SJVAPCD has developed a number of rules and regulations to reduce emissions from existing air pollution sources and to offset the effects of continued Central Valley growth. Many rules are aimed at industrial sources or heavy industries. As the major air pollution sources become better controlled, newer rules focused on smaller sources that are significant pollution contributors on a cumulative scale. The air district is pre-empted from directly controlling on-road vehicles, trains, etc., but does have authority to regulate their impact through "indirect source" rules. The list of APCD rules that are potentially applicable to the proposed project include:

Rule 3135 - Dust Control Plan and Fee
Rule 4102 - Nuisance Prohibition
Rule 4103 - Open Burning Limits on Agricultural Debris
Rule 4641 - Asphalt Emissions Limits
Rule 4901 - Prohibits Wood-Burning Fireplaces Except in Very Low-Density Housing.
Rule 4902 - Requires Low-Nox Water Heaters
Regulation VIII - Fugitive PM-10 Prohibitors
Rule 9510 - Indirect Source Review - Traffic and Construction Emissions Impact Mitigation

AIR QUALITY IMPACTS

THRESHOLDS OF SIGNIFICANCE

Ozone and PM-10 are the two non-attainment pollutants in the air basin that merit critical consideration relative to project-related air quality impacts. While any generation of air pollution is of concern, precursors to ozone and/or PM-10 generation have the most stringent thresholds. For projects within the SJVAB, the SJVAPCD, in its "Guide for Assessing and Mitigating Air Quality Impacts," or GAMAQI (updated 2001), recommends use of the following thresholds for project operation:

ROG	10 tons/year
NOx	10 tons/year
CO	violation of 1- or 8-hour standard

Significance could also derive from emissions of odors or hazardous air pollutants. Development and occupancy of a residential, office or commercial community would not typically generate any hazardous air pollutants or odors. Some odors may result from on-going agricultural operations in the project vicinity. However, nearby agricultural operations are not associated with animal husbandry or occasionally odorous crops such as onions or garlic. The absence of dairies, feed lots, poultry ranches, hog farms, etc., near the site, suggest that agricultural odor is not likely a project siting constraint.

Construction activity is an important PM-10 contributor for new development in the air basin. Because prediction of PM-10 generation depends on a variety of variables which may change from project to project or from day to day, the SJVAPCD has recommended a qualitative, rather than a quantitative, approach to assessing impact significance for PM-10 construction activity emissions. The air district has developed a menu of PM-10 control options in GAMAQI that define the minimum content of a construction dust control program as required by Rule VIII of the district's rules and regulations. In addition to the mandatory program, GAMAQI provides discretionary enhanced or additional control measures that should be implemented if the activity occurs in close proximity to sensitive receptors. With the effective implementation of a minimum dust control program as required by Regulation VIII, and with the use of enhanced or additional measures, where warranted, the PM-10 impact from construction activities is found to less-than-significant. The listing of required measures, as well as those additional candidate measures recommended because of possible proximity of adjacent sensitive receptors, are included in the mitigation section of this report.

Though federal state standards for PM-2.5 have been established, the SJAPCD has not developed a threshold of significance for this pollutant.

CONSTRUCTION ACTIVITY IMPACTS

Construction activities may generate fugitive dust (PM-10) during clearing and grading, and equipment exhaust from earth-moving and construction equipment. The SJAPCD considers reduction of fugitive dust through compliance with all Regulation VIII provisions to be adequate proof that PM-10 emissions from soil disturbance have been reduced to less-than-significant levels. Construction equipment exhaust, however, may impact regional air quality in ways that are not mitigated by Reg. VIII. Diesel-fueled equipment exhaust contains high levels of NOx that participate in regional smog formation. Diesel exhaust also contains diesel particulate matter (DPM) that is a known carcinogen. The Air District has therefore developed mitigation requirements for all major construction projects. A major development is defined as:

- 50 of more residential units
- 2,000 square feet of commercial space
- 39,000 square feet of office space

Reynolds Ranch qualifies as major under every one of these categories. These mitigation requirements are a component of Rule 9510 (adopted December, 2005). Rule 9510 became effective March 1, 2006.

For construction equipment, emissions must be reduced by a specified level compared to the emissions that would have resulted from using statewide average equipment. The emissions for any equipment greater than 50 horse-power (HP) reduction requirement is as follows:

20% of total NOx emissions

45% of total PM-10 emissions

These reductions can be achieved by using less pollutant equipment, or by paying an in-lieu fee, or by a combination of both approaches. The fee is approximately $9,000 per ton for each pollutant.

The SJVAPCD will utilize the collected fees to implement basin-wide pollution control programs such as purchase of cleaner equipment for transit agencies, school districts, etc. Documentation of the calculated construction activity emissions, any "credit" for a commitment to using cleaner equipment (diesel equipment with oxidation catalysts, soot filters, etc.), and any residual excess to be mitigated by payment of fees must be included in an Air Impact Assessment (AIA) required for every major project. The AIA may be prepared by the project applicant, or the APCD will prepare the AIA and fee calculation using default values. The AIA application must be submitted no later than the date of any final discretionary approval by a public agency. Compliance with Rule 9510 requirements for construction equipment exhaust is considered to mitigate exhaust impacts to regional air quality to less-than-significant.

OPERATIONAL ACTIVITY IMPACTS

This project proposed to develop approximately 1,434 dwelling units and approximately 350,000 square feet of commercial development and approximately 200,000 square feet of office space on approximately 220 acres. The project will add 28,300 daily trips to the regional traffic burden at project build-out. Residential use will also generate air emissions from a variety of small sources such as consumer products, paints and coatings, landscape utility equipment, natural gas combustion, cooking or recreational fires, pesticides, etc. These emissions are designated as "area sources" in contrast to the "mobile sources" from project-related travel. Conversion of agricultural uses to residential will eliminate the air pollution emissions associated with crop production that has historically occurred on and around this parcel.

GAMAQI segregates projects into three classes of potential impact with three corresponding analysis levels, as follows:

Small Project Analysis Level (SPAL)

Cursory Analysis Level (CAL)

Full Analysis Level (FAL)

Table 5-2 of the GAMAQI identifies threshold sizes for residential uses. When the GAMAQI was initially developed, a residential project that generates no more than 1,453 daily trips is considered to require only a SPAL. With continuing emissions improvements, the daily trip threshold has increased due to an improved vehicle fleet. However, at 28,300 daily trips, no amount of emissions improvements can reduce the project impact below the significance threshold. The project analysis is therefore at a CAL level of detail.

Components of a CAL include:

- Regional emissions calculations using URBEMIS computer model.
- CO Screening Analysis based on the CALINE4 model.
- Determine if odors, air toxics or hazards such as asbestos may be associated with the project.
- Conduct a FAL for a potentially significant project.

REGIONAL EMISSIONS (URBEMIS2002)

URBEMIS2002 calculations were performed for interim year 2008 and project build-out in the year 2015. The year 2015 was used as a conservative estimate even though build-out may not occur until beyond 2015. Cars are becoming progressively cleaner, such that a build-out assumption of 2015 will predict higher levels of emissions than a later year. Total annual emissions were assumed to be 365 times the annual peak. The URBEMIS2002 model typically includes a winter calculation that includes a large number of wood stoves and operating fireplaces that are not representative of suburban households. The smog problem in the Valley is furthermore a warm season issue. Multiplication of the summer emissions rate by 365 rather than a separate winter calculation was presumed to be more representative of project-related impacts to regional ozone issues.

Tables 5 and 6 summarize the results of these calculations. ROG and NOx will exceed the SJVAPCD significance threshold. Project-related air quality impacts are thus considered individually significant on a basin-wide/regional scale.

Mitigation of significant operational activity air quality impacts is required by SJVAPCD rules and regulations. The district has adopted an Indirect Source Review (ISR) rule that requires an applicant to reduce one-third of its baseline (non-mitigated) NOx emissions for a period of ten years after completion of each project phase. Similarly, one-half of project-related PM-10 emissions must be reduced.

Reduction can occur through on-site measures such as vehicle trip reduction or enhanced energy efficiency. Off-site measures, such as purchase of cleaner equipment or retirement of old "clunkers" is also an option. Finally, payment of an off-site mitigation fee is required for any excess emissions. For example, without any on-site mitigation, the off-site mitigation fee for Phase I is calculated as follows:

NOx = 15.83 tons/year x 2.5 x $9,350/ton = $370,026.25

PM-10 = 14.44 tons/year x 5 x $9,011/ton = $650,594.20

Total = $1,020,620.45

Any quantifiable off-set must be documented in an Air Impact Assessment (AIA) application. The AIA application is due at the APCD on or before the date of any final public agency discretionary action. Phase I will have a large employee base with hundreds of employees living in/near Lodi working the same shift. The potential for car-pooling, van-pooling and other multi-occupant vehicle use is substantial for the proposed project. For example, trip reduction of ten percent would translate into a $100,000 fee reduction. A number of measures could be subsidized by this cost saving. The combination of on-site mitigation measures and in-lieu fees applied to basin-wide mitigation programs will reduce regional air quality impacts to a level that is considered less-than-significant.

Table 5

Interim Year Annual Project Air Pollution Emissions

Pollutant	Phase I Emissions Tons per Year Year 2008	SJVAPCD Threshold
ROG		
Area Sources	6.08	
Mobile Sources	13.34	
TOTAL	19.42	10
NOx		
Area Sources	2.16	
Mobile Sources	13.67	
TOTAL	15.83	10
CO		
Area Sources	2.16	
Mobile Sources	135.33	
TOTAL	137.34	[1]
PM-10		
Area Sources	0.01	
Mobile Sources	14.43	
TOTAL	14.44	[2]

1. Not significant if the one-hour CO standard of 20 ppm or the 8-hour standard of 9 ppm are not exceeded
2. Not significant if all aspects of SJVAPCD Regulation VIII are complied with

Source: URBEMIS2002 Computer Model; Daily rate X 365 days/year ÷ 2,000 lb/ton

Table 6

Year 2015 Project Air Pollution Emissions

Pollutant	Emissions Tons per Year Year 2015	SJVAPCD Threshold
ROG		
Area Sources	19.64	
Mobile Sources	27.38	
TOTAL	47.02	10
NOx		
Area Sources	4.43	
Mobile Sources	29.68	
TOTAL	34.11	10
CO		
Area Sources	5.87	
Mobile Sources	297.58	
TOTAL	303.45	[1]
PM-10		
Area Sources	0.02	
Mobile Sources	61.42	
TOTAL	61.44	[2]

[1] Not significant if the one-hour CO standard of 20 ppm or the 8-hour standard of 9 ppm are not exceeded

[2] Not significant if all aspects of SJVAPCD Regulation VIII are complied with

Source: URBEMIS2002 Computer Model; Daily rate X 365 days/year ÷ 2,000 lb/ton

Air Quality Management Plan Consistency

Regionally, at build-out in year 2030, project implementation will generate 28,300 daily trips to the project. However, it will also provide living space for an estimated 2,400 people, schools to accommodate 1,000 students, as well as office and retail facilities. Because people can live, shop and work in the same neighborhood, as well as have children walk to neighborhood schools and recreational parks, in a regional sense the project is air quality positive.

In the City of Lodi's Housing Element for 2003-2009, adopted in 2004 as part of the General Plan, approximately 5,004 dwelling units were identified for annexation residential development. With its planned 1,084 dwelling units, this project will account for approximately 20 percent of that already planned development. Although the mobile source emissions will have a regionally significant and non-mitigable air quality impact, the air quality benefits of a positive jobs-housing balance contribution should be noted in any statement of overriding considerations.

The basin air quality management plan (AQMD) is based upon the growth forecasts for the region. The AQMD anticipates emissions increases from planned growth, and emissions reductions from existing and future control programs. To the extent that the proposed project is consistent with City of Lodi housing projections, and to the extent that local job generation is air quality positive in reducing out-of-area travel, the project is considered consistent with the AQMP.

CO Screening Analysis

Possible air quality "hot spots" require substantial concentrations of traffic, highly congested traffic flow, and already substantially elevated background CO concentrations. None of these conditions are met near the project site. A number of intersections are forecast to experience substantial congestion without mitigation (signals and widening). A screening analysis for future CO exposures was therefore performed to verify the absence of any future "hot spots" even if traffic mitigation is slow to be implemented. Cars are becoming sufficiently clean, however, such that CO "hot spots" no longer occur.

To verify this conclusion, a CO screening analysis was performed at the intersections surrounding the project. One-hour CO concentrations were calculated on the sidewalks adjacent to these intersections. Peak one-hour levels (ppm above background) were as follows:

One-Hour CO Concentrations (ppm)

Intersections	Existing	Interim	Interim & Project	2030	2030 & Project
AM Peak Hours					
Harney Lane/					
Hutchins St.	0.9	0.8	0.8	0.2	0.3
Stockton St.	0.6	0.6	0.6	0.2	0.2
Cherokee Ln.	0.6	0.7	0.7	0.2	0.2
PM Peak Hour					
Harney Lane/					
Hutchins St.	0.9	0.8	0.8	0.2	0.3
Stockton St.	0.6	0.6	0.7	0.2	0.2
Cherokee Ln.	0.5	0.8	0.6	0.2	0.2

Existing peak one-hour local CO background levels are 0.9 ppm. Combined worst-case background (3.7 ppm in 2004) plus local (0.9 ppm) equate to CO levels of 4.6 ppm which are far below the one-hour standard of 20 ppm. Worst-case one hour levels are even lower than the allowable 8-hour exposure of 9 ppm. Micro-scale impacts are less than significant.

Odors, Dust and Hazardous Air Pollutants

There are no releases of odors or toxic air contaminants associated with the Reynolds Ranch development that would be detectable beyond the site perimeter. However, on-site residential uses may be exposed to chemicals used in on-going agricultural activities near the development. Application of chemicals may create hazardous and nuisance odors and farm operations may also create dust.

Agricultural uses are located immediately west and south of the project site. The railroad tracks separate the on-site residential uses from the agricultural uses to the west. Additionally a mini-storage facility located between the tracks and planned medium-density residential uses will help shield the western perimeter. An agricultural buffer is planned along the southern periphery of the project site. It is presumed that a 6 foot fence would separate the perimeter of the residential development from the adjacent mini-storage and agricultural uses to the south.

These buffers and walls around the perimeter of the project site would minimize potential conflicts in land use. Schools and parks are considered pollution-sensitive, especially for toxic or hazardous compounds sometimes used in agriculture. These uses will be located within the center of the project site in order to maximize the set-back between active agricultural fields and

maximally sensitive land uses. Application and toxicity of agricultural chemicals is also strictly regulated when they are used near homes or schools. Though these measures are believed to adequately shield the project from any adverse impacts, it is recommended that anyone buying or leasing a residential property in Reynolds Ranch be provided a disclosure statement. The notifications should disclose that the residence is located in an agricultural area and is subject to ground and aerial applications of chemicals. The disclosure should note that agricultural operation may, on occasion, create odor and dust nuisances from tilling, harvesting or processing of crops.

MITIGATION

Dust control is required by SJVAPCD Regulation VIII to reduce PM-10 emissions during construction to a less-than-significant level. Table 7 lists the measures that are required in Regulation VIII. Because the SJVAB is a non-attainment area for PM-10, and this is a large development, inclusion of additional dust control measures beyond minimum requirements is required. Table 7 thus includes the menu of recommended additional control measures.

Operational activity emissions are predicted to exceed NOx and ROG significance thresholds for both the interim time period and at project build-out. The degree of "excess" emissions is so large that no feasible mitigation can be adopted to reduce ozone precursor emissions to less than significant.

Micro-scale impacts are less than significant. No air quality "hot spots" will be generated by this project adjacent to the project site.

Adjacent agricultural application of chemicals may create hazardous and nuisance odors and farm operations may also create dust. The planned agricultural buffer along the southern periphery of the property as well as 6 foot wall surrounding the project should provide adequate dust protection for the southern perimeter. The distance separation of the train tracks and mini-storage units should provide adequate protection for the residences on the western perimeter. The mini-storage buildings will also act as dust buffer. A 6 foot wall surrounding residences on the western periphery of the project is recommended for both dust and noise.

Toxicity of chemicals applied near homes, schools and parks as well as application methods will be strictly regulated to achieve a less-than-significant exposure to residents, students and other sensitive on-site users. Anyone buying or leasing a residential property in Reynolds Ranch should be notified in writing that their property is in an agricultural area. The notifications should disclose that the residence is located in an agricultural area and is subject to ground and aerial applications of chemicals. The disclosure should note that agricultural operation may, on occasion, create odor and dust nuisances from tilling, harvesting or processing of crops.

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Table 7
Dust Control Measures for Construction
Emissions of PM-10

Regulation VIII Control Measures

The following controls are required to be implemented at all construction stites to maintain VDE (visible dust emissions) at less than 20 percent opacity as required by Regulation VIII:

- A fugitive dust control plan shall be developed for APCD approval prior to grading.
- A responsible individual trained in dust control shall be identified, and his/her name and contact information shall be conspicuously posted around the perimeter of any grading/construction areas.
- All disturbed areas, including storage piles, which are not being actively utilized for construction purposes, shall be effectively stabilized of dust emissions using water, chemical stabilizer/suppressant, or vegetative ground cover.
- All on-site unpaved roads and off-site unpaved access roads shall be effectively stabilized of dust emissions using water or chemical stabilizer/suppressant.
- All land clearing, grubbing, scrapping, excavation, land leveling, grading, cut and fill, and demolition activities shall be effectively controlled of fugitive dust emissions utilizing application of water or by presoaking.
- When materials are transported off-site, all materials shall be covered, effectively wetted to limit visible dust emissions, or at least six inches of freeboard space from the top of the container shall be maintained.
- All operations shall limit or expeditiously remove the accumulation of mud or dirt from adjacent public streets at least once every 24 hours when operations are occurring. (*The use of dry rotary brushes is expressly prohibited except where accompanied by sufficient wetting to limit the visible dust emissions.) (Use of blowers is expressly forbidden.)*
- Following the addition of materials to, or the removal of materials from, the surface of outdoor storage piles, said piles shall be effectively stabilized of fugitive dust emissions ut8ilizing sufficient water or chemical stabilizer/suppressant.

Additional Control Measures

The following additional control measures are strongly encouraged because the basin is a PM-1-non-attainment area:

- Install wheel washers for all exiting trucks, or wash off all trucks and equipment leaving the site.

- Install wind breaks at windward side(s) of construction areas.
- Suspend excavation and grading activity when winds exceed 20 mph.
- Limit area subject to excavation, grading and other construction activity at any time.

APPENDIX

URBEMIS2002 Computer Model Output

2008

URBEMIS 2002 For Windows 8.7.0

File Name: <Not Saved>
Project Name: Reynolds Ranch - Phase I
Project Location: San Joaquin Valley
On-Road Motor Vehicle Emissions Based on EMFAC2002 version 2.2

SUMMARY REPORT
(Pounds/Day - Summer)

AREA SOURCE EMISSION ESTIMATES

	ROG	NOx	CO	SO2	PM10
TOTALS (lbs/day,unmitigated)	33.29	11.81	11.00	0.00	0.03

OPERATIONAL (VEHICLE) EMISSION ESTIMATES

	ROG	NOx	CO	SO2	PM10
TOTALS (lbs/day,unmitigated)	73.12	74.89	741.54	0.46	79.08

SUM OF AREA AND OPERATIONAL EMISSION ESTIMATES

	ROG	NOx	CO	SO2	PM10
TOTALS (lbs/day,unmitigated)	106.41	86.70	752.54	0.46	79.10

URBEMIS 2002 For Windows 8.7.0

File Name: <Not Saved>
Project Name: Reynolds Ranch - Phase I
Project Location: San Joaquin Valley
On-Road Motor Vehicle Emissions Based on EMFAC2002 version 2.2

DETAIL REPORT
(Pounds/Day - Summer)

AREA SOURCE EMISSION ESTIMATES (Summer Pounds per Day, Unmitigated)

Source	ROG	NOx	CO	SO2	PM10
Natural Gas	0.86	11.80	9.44	0	0.02
Hearth - No summer emissions					
Landscaping	0.25	0.01	1.56	0.00	0.01
Consumer Prdcts	7.34	-	-	-	-
Architectural Coatings	24.84	-	-	-	-
TOTALS(lbs/day,unmitigated)	33.29	11.81	11.00	0.00	0.03

UNMITIGATED OPERATIONAL EMISSIONS

	ROG	NOx	CO	SO2	PM10
Medium density residentia	9.51	11.07	110.37	0.07	11.68
Office park	63.61	63.83	631.17	0.39	67.39
TOTAL EMISSIONS (lbs/day)	73.12	74.89	741.54	0.46	79.08

Does not include correction for passby trips.
Does not include double counting adjustment for internal trips.

OPERATIONAL (Vehicle) EMISSION ESTIMATES

Analysis Year: 2008 Temperature (F): 85 Season: Summer

EMFAC Version: EMFAC2002 (9/2002)

Summary of Land Uses:

Unit Type	Acreage	Trip Rate	No. Units	Total Trips
Medium density residentia	9.38	6.00 trips/dwelling unit	150.00	900.00
Office park		3.31 trips/Emplyee	1,600.00	5,296.00
		Sum of Total Trips		6,196.00
		Total Vehicle Miles Traveled		52,085.80

Vehicle Assumptions:

Fleet Mix:

Vehicle Type	Percent Type	Non-Catalyst	Catalyst	Diesel
Light Auto	55.00	1.60	98.00	0.40
Light Truck < 3,750 lbs	15.00	2.70	95.30	2.00
Light Truck 3,751- 5,750	16.20	1.20	97.50	1.30
Med Truck 5,751- 8,500	7.20	1.40	95.80	2.80
Lite-Heavy 8,501-10,000	1.10	0.00	81.80	18.20
Lite-Heavy 10,001-14,000	0.40	0.00	50.00	50.00
Med-Heavy 14,001-33,000	1.00	0.00	20.00	80.00
Heavy-Heavy 33,001-60,000	0.90	0.00	11.10	88.90
Line Haul > 60,000 lbs	0.00	0.00	0.00	100.00
Urban Bus	0.20	0.00	50.00	50.00
Motorcycle	1.70	76.50	23.50	0.00
School Bus	0.10	0.00	0.00	100.00
Motor Home	1.20	8.30	83.30	8.40

Travel Conditions

	Residential			Commercial		
	Home-Work	Home-Shop	Home-Other	Commute	Non-Work	Customer
Urban Trip Length (miles)	10.8	7.3	7.5	9.5	7.4	7.4
Rural Trip Length (miles)	16.8	7.1	7.9	14.7	6.6	6.6
Trip Speeds (mph)	35.0	35.0	35.0	35.0	35.0	35.0
% of Trips - Residential	32.9	18.0	49.1			
% of Trips - Commercial (by land use)						
Office park				48.0	24.0	28.0

Changes made to the default values for Land Use Trip Percentages

The Trip Rate and/or Acreage values for Apartments low rise have changed from the defaults 6.9/9.38 to 6.0/9.38

Changes made to the default values for Area

Changes made to the default values for Operations

The operational emission year changed from 2005 to 2008.

2015

URBEMIS 2002 For Windows 8.7.0

File Name: <Not Saved>
Project Name: Reynolds Pase 2
Project Location: San Joaquin Valley
On-Road Motor Vehicle Emissions Based on EMFAC2002 version 2.2

SUMMARY REPORT
(Pounds/Day - Summer)

AREA SOURCE EMISSION ESTIMATES

	ROG	NOx	CO	SO2	PM10
TOTALS (lbs/day,unmitigated)	107.59	24.26	32.18	0.11	0.10

OPERATIONAL (VEHICLE) EMISSION ESTIMATES

	ROG	NOx	CO	SO2	PM10
TOTALS (lbs/day,unmitigated)	150.05	162.65	1,630.55	1.93	336.53

SUM OF AREA AND OPERATIONAL EMISSION ESTIMATES

	ROG	NOx	CO	SO2	PM10
TOTALS (lbs/day,unmitigated)	257.64	186.91	1,662.72	2.04	336.63

URBEMIS 2002 For Windows 8.7.0

File Name: <Not Saved>
Project Name: Reynolds Pase 2
Project Location: San Joaquin Valley
On-Road Motor Vehicle Emissions Based on EMFAC2002 version 2.2

DETAIL REPORT
(Pounds/Day - Summer)

AREA SOURCE EMISSION ESTIMATES (Summer Pounds per Day, Unmitigated)

Source	ROG	NOx	CO	SO2	PM10
Natural Gas	1.80	24.17	16.39	0	0.04
Hearth - No summer emissions					
Landscaping	2.45	0.09	15.78	0.11	0.06
Consumer Prdcts	53.03	-	-	-	-
Architectural Coatings	50.31	-	-	-	-
TOTALS(lbs/day,unmitigated)	107.59	24.26	32.18	0.11	0.10

UNMITIGATED OPERATIONAL EMISSIONS

	ROG	NOx	CO	SO2	PM10
Single family housing	5.38	6.23	64.64	0.07	12.94
Medium density residentia	16.71	17.45	180.92	0.21	36.23
High density residential	7.11	7.48	77.55	0.09	15.53
MDR residential-Phase 1	5.33	5.61	58.17	0.07	11.65
HDR senior residential	3.53	3.11	32.28	0.04	6.46
Elementary school	14.23	7.97	79.51	0.09	16.48
Mini storage	0.80	1.08	10.60	0.01	2.24
Commercial	59.95	81.35	794.60	0.96	167.79
Office park	37.01	32.37	332.28	0.39	67.19
TOTAL EMISSIONS (lbs/day)	150.05	162.65	1,630.55	1.93	336.53

Does not include correction for passby trips.
Does not include double counting adjustment for internal trips.

OPERATIONAL (Vehicle) EMISSION ESTIMATES

Analysis Year: 2015 Temperature (F): 85 Season: Summer

EMFAC Version: EMFAC2002 (9/2002)

Summary of Land Uses:

Unit Type	Acreage	Trip Rate	No. Units	Total Trips
Single family housing	34.33	9.71 trips/dwelling unit	103.00	1,000.13
Medium density residentia	30.06	5.82 trips/dwelling unit	481.00	2,799.42
High density residential	5.26	6.00 trips/dwelling unit	200.00	1,200.00
MDR residential-Phase 1	2.42	6.00 trips/dwelling unit	150.00	900.00
HDR senior residential	30.00	3.33 trips/dwelling unit	150.00	499.50
Elementary school		1.40 trips/students	1,000.00	1,400.00
Mini storage		37.74 trips/acre	5.30	200.02
Commercial		42.86 trips/1000 sq. ft.	350.00	15,001.00
Office park		3.31 trips/employee	1,600.00	5,296.00
		Sum of Total Trips		28,296.07
		Total Vehicle Miles Traveled		222,374.19

Vehicle Assumptions:

Fleet Mix:

Vehicle Type	Percent Type	Non-Catalyst	Catalyst	Diesel
Light Auto	54.40	0.40	99.40	0.20
Light Truck < 3,750 lbs	15.30	0.70	98.00	1.30
Light Truck 3,751- 5,750	16.40	0.60	98.80	0.60
Med Truck 5,751- 8,500	7.30	0.00	98.60	1.40
Lite-Heavy 8,501-10,000	1.10	0.00	81.80	18.20
Lite-Heavy 10,001-14,000	0.30	0.00	66.70	33.30
Med-Heavy 14,001-33,000	1.00	0.00	20.00	80.00
Heavy-Heavy 33,001-60,000	0.80	0.00	0.00	100.00
Line Haul > 60,000 lbs	0.00	0.00	0.00	100.00
Urban Bus	0.20	0.00	50.00	50.00
Motorcycle	1.60	50.00	50.00	0.00
School Bus	0.10	0.00	0.00	100.00
Motor Home	1.50	0.00	93.30	6.70

Travel Conditions

	Residential			Commercial		
	Home-Work	Home-Shop	Home-Other	Commute	Non-Work	Customer
Urban Trip Length (miles)	10.8	7.3	7.5	9.5	7.4	7.4
Rural Trip Length (miles)	16.8	7.1	7.9	14.7	6.6	6.6
Trip Speeds (mph)	35.0	35.0	35.0	35.0	35.0	35.0
% of Trips - Residential	32.9	18.0	49.1			
% of Trips - Commercial (by land use)						
Elementary school				20.0	10.0	70.0
Mini storage				2.0	1.0	97.0
Commercial				2.0	1.0	97.0
Office park				48.0	24.0	28.0

Changes made to the default values for Land Use Trip Percentages

The Trip Rate and/or Acreage values for Single family housing have changed from the defaults 9.57/34.33 to 9.71/34.33
The Trip Rate and/or Acreage values for Apartments low rise have changed from the defaults 6.9/30.06 to 5.82/30.06
The Trip Rate and/or Acreage values for Apartments mid rise have changed from the defaults 5.76/5.26 to 6.0/5.26
The Trip Rate and/or Acreage values for Apartments high rise have changed from the defaults 5.29/2.42 to 6.0/2.42
The Trip Rate and/or Acreage values for Retirement community have changed from the defaults 3.71/30. to 3.33/30.

Changes made to the default values for Area

Changes made to the default values for Operations

The operational emission year changed from 2005 to 2015.

SOUTH COAST AIR QUALITY MANAGEMENT DISTRICT

THE HEALTH EFFECTS OF AIR POLLUTION ON CHILDREN

Fall 2000

Michael T. Kleinman, Ph.D.
Professor, Department of Community and Environmental Medicine
University of California, Irvine.

Table of Contents

Introduction

Air pollution has many effects on the health of both adults and children. The purpose of this article will be to examine what is known about how air pollution affects health, especially children's.

Over the past several years the incidence of a number of diseases has increased greatly. Asthma is perhaps the most important disease with an increasing incidence, but other diseases, such as allergic reactions, bronchitis and respiratory infections also have been increasing. The cause of these increases may be due at least in part to the effects of air pollution. This review will address the following questions:

1. Why are children more susceptible to the effects of air pollution than adults?
2. Which air pollutants have the greatest impact on the health of children and adults?
3. What can be done to reduce the effects of air pollution on children's health?

Why are Children More Susceptible to Air Pollution Than Adults?

In many health effects research studies, children are considered as if they were small adults. This is not really true. There are many differences between children and adults in the ways that they respond to air pollution. For example, children take in more air per unit body weight at a given level of exertion than do adults. When a child is exercising at maximum levels, such as during a soccer game or other sports event, they may take in 20 percent to 50 percent more air -- and more air pollution -- than would an adult in comparable activity.

Another important difference is that children do not necessarily respond to air pollution in the same way as adults. Adults exposed to low levels of the pollutant ozone will experience symptoms such as coughing, soreness in their chests, sore throats, and sometimes headaches. Children, on the other hand, may not feel the same symptoms, or at least they do not acknowledge them when asked by researchers. It is currently not known if children actually do not feel the symptoms or if they ignore them while preoccupied with play activities.

This probably does not mean that children are less sensitive to air pollution than adults. There are several good studies that show children to have losses in lung functions even when they don't cough or feel discomfort. This is important because symptoms are often warning signals and can be used to trigger protective behavior. Children may not perceive these warning signals and might not reduce their activities on smoggy days.

Children also spend more time outside than adults. The average adult, except for those who work mostly outdoors, spends most of their time indoors -- at home, work, or even at the gym. Children spend more time outside, and are often outdoors during periods when air pollution is at its highest.

The typical adult spends 85 percent to 95 percent of their time indoors, while children may spend less than 80 percent of their time indoors. Children may also exert themselves harder than adults when playing outside.

Perhaps the most important difference between adults and children is that children are growing and developing. Along with their increased body size, children's lungs are growing and changing, too.

The Lung's Important Role in Health
The lung is an extremely complex organ. While most organs in your body are made up of a few different types of cells, the lung contains more than 40 different kinds of cells. Each of these cells is important to health and maintaining the body's fitness.

Air pollution can change the cells in the lung by damaging those that are most susceptible. If the cells that are damaged are important in the development of new functional parts of the lung, then the lung may not achieve its full growth and function as a child matures to adulthood. Although very little research has been conducted to address this extremely important issue, this review will discuss the information that is available.

USC Children's Health Study
Recent results from the Children's Health Study, conducted by investigators at the University of Southern California, suggest that children with asthma are at much greater risk of increased asthma symptoms when they live in communities with higher levels of ozone and particles and participate in three or more competitive sports. Having said all this, the purpose of this review is not to discourage children or adults from normal daily activities and outdoor exercise. Exercise has very important, beneficial outcomes. Appropriate exercise and prudent exposures of children and adults should be encouraged even in an environment that may always contain some amount of air pollution.

Which Air Pollutants Have the Greatest Impact on the Health of Children and Adults?

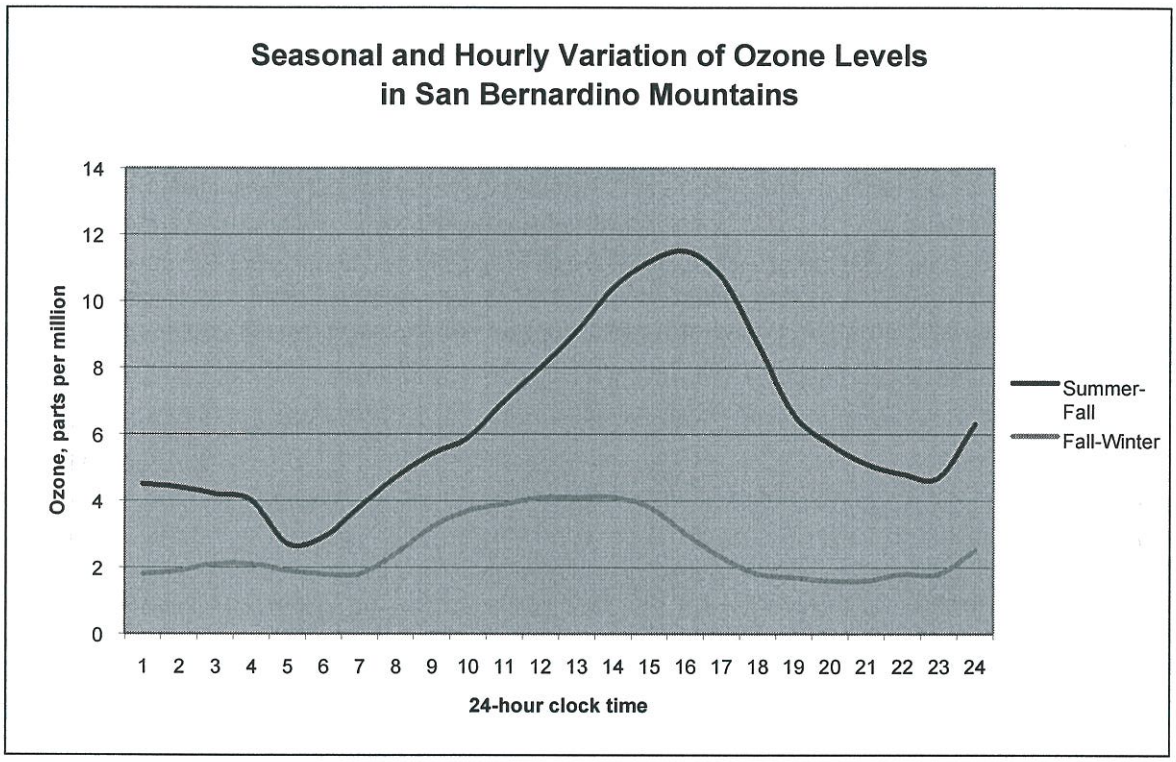
Ozone

Ozone is one of the most important air pollutants affecting human health in regions like Southern California.

Ozone (O_3) is a molecule built of three atoms of oxygen linked together in a very energetic combination. When ozone comes into contact with a surface it rapidly releases this extra force in the form of chemical energy. When this happens in biological systems, such as the respiratory tract, this energy can cause damage to sensitive tissues in the upper and lower airways.

Ozone formation

Because ozone forms as a product of solar energy and photochemical reactions of pollutants, it is not surprising that the highest concentrations of ozone in the atmosphere occur when sunlight is most intense. Thus, ozone generally reaches peak levels during the middle of the day in the summer months. These types of air pollution patterns are called diurnal and seasonal variations. The following graph shows that ozone levels in the San Bernardino Mountains are highest in the summer and fall, and peak in the late afternoon.



Ozone Air Quality Standards

Federal and state agencies have set air quality standards for ozone. An ozone level greater than 0.08 parts per million (ppm) averaged over eight hours is considered unhealthful. This level has been set because both laboratory and community studies have demonstrated measurable effects of ozone at or above that threshold.

The effects of ozone on people include:

- irritation of the nose and throat;
- increased mucus production and tendency to cough;
- eye irritation and headaches for some; and
- during severe episodes, chest pain and difficulty taking a deep breath without coughing.

How Ozone Damages Lungs

What happens when you breathe air that is contaminated with ozone? Like oxygen, ozone is soluble in the fluids that line the respiratory tract. Therefore some ozone can penetrate into the gas-exchange, or alveolar, region of the deep lung.

The following photos show how ozone affects the sensitive tissue in the deep lung. The pictures are from the lungs of rats exposed to ozone in a laboratory under carefully controlled conditions. The human lung is similar --although not identical -- to the rat's lung in terms of the types of cells and the overall structure of the alveolar region.

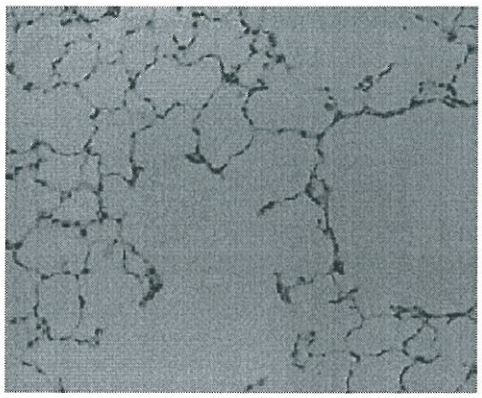


Figure 1

Figure 1 shows a magnified view of the structure of the normal gas-exchange region of the lung. It is called the gas-exchange region because oxygen inhaled from the air is transferred to the hemoglobin in blood in small blood vessels located inside the thin walls separating the alveolar air spaces.

At the same time, carbon dioxide, produced by normal metabolism and dissolved in the blood, is excreted into the air and expired when you breathe out.

The walls of a normal alveolus are very thin. There are only two layers of cells and a thin interstitial matrix separating the air in the alveolar space, or lumen, from the fluid inside the blood vessels. The cells that line the healthy alveoli are mostly very broad and very thin, and are called Type I lung cells or Type I pneumocytes. This provides a very large surface area across which gases can be efficiently transported.

Figure 2 shows the effects of breathing 0.2 ppm ozone for 4 hours. In Southern California air pollution levels can approach 0.2 ppm -- a Stage 1 ozone alert -- during the smoggiest summer days. The photo shows evidence of additional cells, called macrophages, and some material that may be fragments of ozone-injured alveolar wall cells inside the alveolar space.

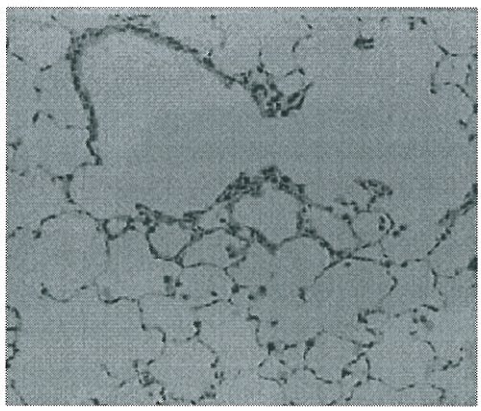


Figure 2

Macrophages are immune system cells that respond to the injury of the delicate cells that line the alveolar lumen. These macrophages play important roles in protecting the lungs from inhaled bacteria,

fungi and viruses, and are also important in helping to repair lung tissue injury caused by inhaled pollutants.

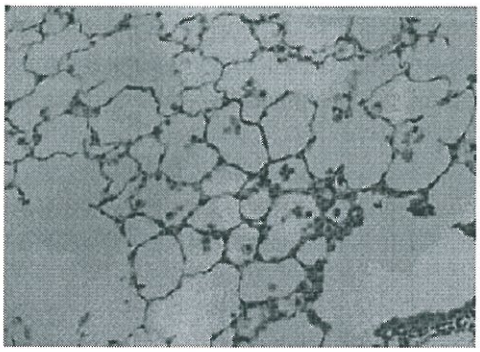


Figure 3

Figure 3 shows more extensive damage following exposure a higher concentration of ozone, 0.6 ppm. The alveolar walls are thicker and there is evidence of cells infiltrating within the walls. There are more macrophages in the alveolar spaces and the thin, Type I cells have been damaged and replaced with thicker Type II, almost cube-shaped cells that are more resistant to the toxic effects of ozone. All of these changes occurred within 48 hours after exposure. If exposure continues for more than three days, the evidence of cell injury seems to be reduced, except for the continuing presence of the Type II cells.

Is Ozone-Related Lung Damage Permanent?
People actually report that the symptoms they feel when first exposed to ozone seem to go away, even though their exposure continues.

Following ozone injury, if the lung is not exposed to ozone for approximately five to seven days, it can for the most part repair itself provided the injury is not too extensive. However, long-term studies with laboratory animals have shown that there may be residual and in some cases permanent damage. This damage might be thought of as accelerated aging of the lung. Thus, frequent exposures to ozone can cause transient damage. The lung's defenses can repair most but probably not all of that damage within a relatively short time in most healthy individuals.

Research and Air Quality Standards
Health scientists probably know more about the effects of ozone on human health than about any other pollutants. This is because ozone is pervasive in the environment. Also there are excellent methods of measuring ozone so the pollutant can be studied using epidemiological methods. The findings of these epidemiological studies can be verified using well-controlled laboratory studies with human volunteers and laboratory animals. Thousands of scientific papers on the health effects of ozone have been published and these have been critically reviewed in documents that provide the scientific basis for National and State Ambient Air Quality Standards. (Ambient refers to outdoor air.)

These so-called Criteria Documents are important because they are extensively reviewed by scientists, public agencies, industry representatives, environmental groups such as the American Lung Association and the Natural Resources Defense Council,

and the public. National and state ambient air quality standards set the goals for healthy air quality in Southern California and across the country.

Based upon the most recent studies, it is now apparent that ozone plays an important role in causing acute health effects, such as heightening asthma symptoms and developing bronchitis symptoms.

The role of ozone in producing long-term or chronic effects is less clear, at least from the available epidemiological studies. However, laboratory animal studies suggest that there can be long-term consequences.

How to Reduce Ozone Exposure
The U.S. Environmental Protection Agency (EPA) has recommended that ozone should not exceed 0.08 ppm averaged over an 8-hr period. When ozone exceeds this level, active children and adults, those with respiratory disease such as asthma, and other people with unusual susceptibility to ozone should limit prolonged outdoor exposure.

Incidentally, personal tobacco smoking during periods of high ozone exposure doubled the risk of asthmatic individuals needing to go to the emergency room for treatment of asthma symptoms.

Carbon Monoxide

Carbon monoxide (CO), a colorless, odorless gas, is a byproduct of combustion.

When inhaled, carbon monoxide reacts very rapidly with hemoglobin in the blood, preventing uptake and transport of oxygen. Because carbon monoxide readily and firmly attaches to hemoglobin, it stays in the blood for a relatively long time. Thus, during an exposure carbon monoxide concentrations in blood can rise in a matter of minutes, then stay high for hours.

Who is Most Sensitive to the Health Effects of Carbon Monoxide?
Most of the health effects directly associated with carbon monoxide are most likely due to decreases in oxygen delivery to vital organs such as the heart and the brain.

People with heart disease may be especially sensitive to the effects of carbon monoxide. In addition, people with lung diseases that limit efficient use of inhaled oxygen, such as asthma and emphysema, may also be susceptible. Even in people without heart or lung diseases, reduced delivery of oxygen to skeletal muscles, especially during exercise, can reduce the ability to perform strenuous work.

At high levels of carbon monoxide exposure, impaired delivery of oxygen to the central nervous system can reduce the ability to respond quickly to external stimuli. After exposures that convert 5 percent to 10 percent of the circulating hemoglobin to carboxyhemoglobin (COHb), people's ability to recognize and react to flashes of light in a test system are reduced. At 10 percent to 30 percent carboxyhemoglobin, nausea,

headaches, unconsciousness, and sometimes death can result. The severity of symptoms increases with the concentration of carboxyhemoglobin.

Air Quality Standards for Carbon Monoxide
Both the EPA and the State of California have set air quality standards for carbon monoxide based on the results of epidemiological and laboratory findings. Ambient levels of carbon monoxide should not exceed 9 ppm, when averaged over an 8-hour interval, and should not exceed 20 ppm in any one-hour period. (The USEPA has a slightly higher 1-hour standard of 35 ppm).

Sources of Carbon Monoxide
The major sources of carbon monoxide pollution are automotive exhaust and emissions from large industrial combustion sources such as electrical power plants. Because these sources produce many contaminants in addition to carbon monoxide -- such as fine particles and nitrogen oxides -- it is often difficult to isolate the health effects of ambient carbon monoxide from those of other pollutants.

In addition to carbon monoxide generated outside, there are also important indoor sources of the pollutant. The most important of these are combustion sources such as gas ovens, gas burners, water heaters, and heating systems. However, in most cases emissions from well-maintained and vented gas appliances are small.

Tobacco smoking is a more significant source of carbon monoxide. Tobacco smoke can contain very high concentrations of carbon monoxide (1,000 ppm to 50,000 ppm). Carbon monoxide levels in the homes of children whose relatives smoke tobacco products can be higher than the carbon monoxide levels outdoors.

Health Effects of Carbon Monoxide
There are hundreds of cases per year of deaths or severe illness due to carbon monoxide poisoning from faulty appliances, indoor emissions of automobile exhaust and industrial exposures. These cases show that carbon monoxide poisoning causes symptoms very similar to those of the flu. In fact, the true number of cases is not really known because many people may have been poisoned slightly and thought that they were just fighting off a cold or the flu. Thus it is very important to make sure that home appliances are well-maintained and that all combustion sources are properly vented to the outdoors.

Epidemiological studies have shown significant association between several health effects and carbon monoxide, although as mentioned earlier it is difficult to completely isolate carbon monoxide's effects from those of other air pollutants.

For example, asthmatic children in Taiwan who were exposed to high levels of traffic-related air pollution -- using carbon monoxide and nitrogen dioxide as marker compounds-- reported more respiratory symptoms than children with lower exposures.

A study of physician office visits in London showed associations between air pollution and doctor visits for asthma and other lower respiratory disease. For children, levels of nitrogen dioxide, carbon monoxide, and sulfur dioxide were associated with increased numbers of medical consultations. However, in adults, the only consistent association was with levels of airborne particles. This suggests that children and adults might respond differently to pollution exposures.

Prenatal Effects of Carbon Monoxide

Carbon monoxide may also have prenatal effects. Pregnant women who were exposed to high levels of ambient carbon monoxide (5 ppm to 6 ppm) were at increased risk of having low birth-weight babies. It has long been known that women who smoke cigarettes during pregnancy have low birth-weight babies, but this is the first study of similar findings in women exposed to environmental carbon monoxide.

Babies exposed to carbon monoxide during the maturation of their organs may suffer permanent changes to those organs. Studies using newborn rats showed that carbon monoxide exposure could cause changes in the heart muscle tissue. This is turn could increase the severity of effects of artery constrictions when they became adults. Other animal studies have shown that long-term carbon monoxide exposure can contribute to a disease called ventricular hypertrophy, in which the cells of the heart's ventricle chambers are enlarged and possibly weakened.

Airborne Particles

Particles, including nitrates, sulfates, carbon[1] and acid aerosols[2] are a complex group of pollutants.

Unlike ozone, which has a specific chemical composition, airborne particles vary in size and composition depending on time and location. Although the components of particles may have common sources, the types and amounts of particles collected at any one time and location may be unique.

To add to the problem, gaseous pollutants including ozone, sulfur dioxide, nitrogen dioxide and carbon monoxide often are present in the atmosphere at the same time as are particles. It is not always possible to clearly differentiate between the health effects of the gases, the particles, and possibly the combination of particles and gases. This complexity presents a tremendous challenge to the scientific community and to public in trying to understand how inhaled particles affect human health.

The Challenge of Measuring Particle Pollution

Precisely measuring particulate pollution is more difficult and labor intensive than measuring gaseous pollutants such as ozone. For this reason, particle concentrations are not measured on a daily basis in most communities. Frequently, they are measured once every six days.

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[1] Both elemental and organic. Elemental carbon is pure carbon from combustion sources, including diesel particulate. Organic carbon is a semi-volatile hydrocarbon from combustion and some evaporative sources.

[2] Aerosol is the scientific term used to describe particles suspended in a fluid, such as air.

Particle samples are collected on filters that are then weighed. Particle concentrations are reported in terms of micrograms of particles per cubic meter ($\mu g/m^3$) of collected air.

Originally, the particle samples were relatively indiscriminate with respect to particle size and often contained very large particles. These large particles contributed a great deal to the weighed particle mass, but might not have been very important with respect to lung health. This is because most of the particles were too large to penetrate through the nasal and head airways to reach the lung. A more health-related sample was needed.

After a great deal of scientific consideration it was decided that particulate matter with aerodynamic diameters[3] less than or equal to 10 microns (μm) should be collected. Ambient air quality standards were developed for this material, which is called PM_{10}.

Sources of Particle Pollution

Researchers noted that the sources of relatively large-size particles (greater than 3 microns in aerodynamic diameter) were quite distinct from the sources of particles less than 1 micron in diameter.

The larger, so-called "coarse" particles are mostly produced by mechanical processes, such as automobile tire wear on the road, industrial cutting, grinding and pulverizing processes and re-suspension of particles from the ground or other surfaces by wind and human activities. The chemical composition of coarse particles may be somewhat similar to the chemical composition of soil in that area, along with industrial compounds from activities such as mining or smelting operations. The coarse fraction of urban aerosols also contains bits of plants, molds, spores and some bacteria. Thus the characteristics of the coarse particles may vary greatly in different communities.

In contrast, the smaller or so-called "fine" particles in the urban aerosol come from combustion sources, such as power plants, automobile, truck, bus and other vehicle exhaust or from the reactions that transform some of the pollutant gases into solid or liquid particles. These distinctions may be important because the current air pollution health effects literature suggests, although not with certainty, that for some key health effects the fine particles are more important than the coarse particles. These findings have led EPA to propose a new nationwide $PM_{2.5}$ standard that would reduce exposure to particles that are 2.5 microns or less in diameter.

Historic Air Pollution Disasters

Epidemiological studies have consistently associated adverse health effects with exposures to particulate air pollution. Early studies implicated particulate and sulfur dioxide pollution in the acute illnesses and premature deaths associated with extremely

[3] Aerodynamic diameter is used to define particles' size. Particle deposition on a surface, or in the lung, depends on the particle's aerodynamic and diffusion characteristics. A particle's aerodynamic characteristics depend on its density, shape, actual size, and velocity while its diffusion characteristics are functions of its size and the density of the air in which it is suspended.

severe pollution episodes in Donora, Penn., London, and New York in the 1940s, 1950s, and 1960s. The particle levels in a four-week pollution disaster in London in 1955 were more than 50 times higher than the California standard.[4] Twenty percent of that aerosol was composed of acid sulfates -- probably sulfuric acid. The number of people hospitalized for lung or heart-related diseases was extraordinarily high, but more importantly there were more than 4,000 premature, or "excess," deaths in the London population.

Fortunately, major efforts by government agencies, the public, and industries have made it very unlikely there will ever be a similar episode in modern urban communities. However, the lessons learned from these disasters are still relevant. Despite the fact that our levels of airborne particles are much lower than those that occurred during the disasters, EPA estimates that there are still more than 6,000 excess deaths in the United States that could be associated with inhaled particles.

Health Effects of Particulate Pollution

Current ambient levels of PM_{10} -- 30 to 150 micrograms per cubic meter -- are associated with increases in the numbers of people that die daily from heart or lung failure. Most of these deaths are among the elderly. However there is a strong body of evidence that some children are also adversely affected by particulate matter.

The American Thoracic Society's Environmental and Occupational Health Assembly reviewed current health effects literature. They report that daily fluctuations in PM_{10} levels have been related to:

- acute respiratory hospital admissions in children;
- school and kindergarten absences;
- decreases in peak lung air flow rates in normal children; and
- increased medication use in children and adults with asthma.

The USC Children's Health Study suggests that children with asthma living in a community with high particle concentrations may have suppressed lung growth. After children moved into cleaner cities their lung growth returned to the normal rate, but they did not recover the lost potential growth, according to John Peters, the study's principle investigator.

It is difficult to positively assign a quantitative risk associated with particulate matter because nearly all studies of its health effects find other pollutants present that may account for some of the effects.

Part of the problem is due to the nature of the data being collected. The levels of particulate matter vary during the course of the day and peak values can be quite high. Few studies have evaluated the effect of these short-term "spikes." However, at least one epidemiological study of children with asthma suggested that changes in symptoms

[4] The California standard for particulate matter (PM_{10}) is 50 micrograms per cubic meter averaged over 24 hours

and lung function correlate more strongly with 1-hour peaks than with 24-hour average concentrations.

Other studies, primarily with laboratory animals, suggest that the chemical composition[5] and surface areas of the particles may be more important than particle mass. Scientists are continuing to study the health effects of particles and are developing better methods for measuring the important constituents. It may be possible in the near future to more accurately assess the effects of inhaled particles on human health.

Nitrogen Oxides

Nitrogen oxides are produced during most combustion processes. Mobile sources and power plants are the major contributors in Southern California.

About 80 percent of the immediately released nitrogen oxide is in the form nitric oxide (NO). Small amounts of nitrous oxide (N_2O) are also produced. Nitrous oxide is a "greenhouse" gas that is suspected of playing an important role in global warming.

Nitric oxide reacts with oxygen in the air to produce nitrogen dioxide (NO_2). Further oxidation during the day causes the nitrogen dioxide to form nitric acid and nitrate particles. In the dark, nitrogen dioxide can react with ozone and form a very reactive free radical. The free radical then can react with organic compounds in the air to form nitrogenated organic compounds, some of which have been shown to be mutagenic and carcinogenic.

Health Effects of Nitrogen Dioxide

Nitrogen dioxide is the most important nitrogen oxide compound with respect to acute adverse health effects. Under most chemical conditions it is an oxidant, as is ozone. However, it takes about 10 times more nitrogen dioxide than ozone to cause significant lung irritation and inflammation.

Nitrogen dioxide differs from ozone in that it suppresses the immune system to a much greater degree. As discussed below, some epidemiological studies have shown that children exposed to high levels of ambient nitrogen dioxide may be at increased risk of respiratory infections. Studies with laboratory animals have indeed shown that if mice are exposed first to nitrogen dioxide and later to bacteria at a level that would not infect a healthy control animal, their normal lung defense mechanisms are suppressed and the bacteria are able to infect the host.

[5] The idea that all particles are equally toxic is not scientifically justified. There are many good examples that can be taken from studies of particles in the workplace. For example, certain types of particles that contain quartz --a natural mineral composed of silicon dioxide but with a specific crystal structure -- are very potent lung irritants. Repeated exposures to this material can lead to a serious, permanent lung disease called lung fibrosis. Other mineral particles that are fibrous, such as specific forms of asbestos, can cause lung cancer. Other particles such as titanium dioxide do not seem to cause occupational diseases.

Average levels of nitrogen dioxide in the United States range from 0.02 to 0.04 ppm. Levels in major urban areas in Southern California may be higher, but the region has not exceeded the federal standard[6] for nitrogen dioxide since 1991.

During the 1970s, one of the first studies relating respiratory illnesses and changes in lung function to ambient nitrogen dioxide concentrations reported that children living in areas with high nitrogen dioxide concentrations had greater incidences of lung-related illness than children living in areas with lower concentrations. Since then, other epidemiological studies have suggested that children with asthma are more likely than children without asthma to have reduced lung function and symptoms of respiratory irritation, such as cough and sore throat, when outdoor average nitrogen dioxide concentrations exceed about 0.02 ppm.

Some studies also have suggested that children younger than five years old may be more severely affected by nitrogen dioxide than older children. Several epidemiological studies have suggested that for children, the most important effect of ambient exposure to nitrogen dioxide might be increased susceptibility to respiratory infections and increased severity of responses to inhaled allergens.

Although many epidemiological studies show significant associations between outdoor nitrogen dioxide concentrations and adverse health outcomes, some studies do not corroborate these effects. In part, this is because it is often difficult to fully account for the influences of indoor sources of nitrogen dioxide.

Improvements in Nitrogen Dioxide Measurements

More recent studies have used special devices, called passive dosimeters, that can be worn by children to collect nitrogen dioxide for later analysis. These measurements give epidemiologists the ability to better assess a child's total nitrogen dioxide exposure over the course of the day. These studies show that there can be a great deal of individual variation in exposures, even for children living in the same communities. Thus, it is not surprising that epidemiological studies that do not estimate a nitrogen dioxide dose may reach different conclusions.

However, laboratory studies involving controlled exposures of human volunteers and laboratory animals have demonstrated plausible effects of nitrogen dioxide on human health. For example, if one exposes rats or other animals to nitrogen dioxide, and then examines their respiratory tract tissues, it is very evident that the pollutant can cause short-term injury similar to that seen after ozone exposure.

Long-term exposures to high concentrations of nitrogen dioxide can produce chronic damage to respiratory tract tissue that resembles the lung disease emphysema.

The pollutant's suppression of immune system functions reduces the ability of the host to fight off bacterial and viral infections. Human volunteers who inhaled weakened

[6] 0.053 ppm as an annual average

influenza virus after being exposed to nitrogen dioxide in laboratories were more susceptible to the infection than a control group that did not inhale nitrogen dioxide.

Other studies show that nitrogen dioxide decreases the body's ability to generate antibodies when challenged by pathogens, and may reduce the ability of the respiratory system to remove foreign particles such as bacteria and viruses from the lung.

Lead

People can be exposed to lead (Pb) through air, food and water. Lead is a toxic heavy metal that causes nerve damage and impairs the body's ability to make hemoglobin, leading to a form of anemia.

Sources of Lead Pollution

Large amounts of lead were emitted to the atmosphere when it was used as a gasoline additive.[7] The emitted lead could be inhaled. In addition, lead fallout from the air caused widespread contamination of soil, plants, food products, and water.

Lead is often measured in children's blood as an index of environmental exposure. Even low levels[8] of lead in the blood of children aged 6 to 7 are linked to measurable changes in intelligence quotient and certain perceptual-motor skills. Higher levels of lead exposure can also result in kidney damage and may be related to high blood pressure in adults.

Sulfur Oxides

Most manmade emissions of the gas sulfur dioxide (SO_2) come primarily from the combustion of fossil fuels such as coal, oil, and diesel fuel.

Most of the sulfur in fossil fuel is converted sulfur dioxide, but a small amount is also converted to sulfuric acid. In the atmosphere, gaseous sulfur dioxide can also be converted to sulfuric acid and sulfate-containing particles. Thus, atmospheric concentrations of sulfur dioxide are often highly associated with acidic particles, sulfuric acid particles and sulfate particle concentrations.

The current National Ambient Air Quality Standards for sulfur dioxide are 18 micrograms per cubic meter averaged annually, and 365 micrograms per cubic meter averaged over 24 hours. Southern California does not exceed the national air quality standard because its industries primarily burn low-sulfur fuels such as natural gas. Much of the sulfur oxide air pollution in Southern California is likely to be associated with diesel emissions.

[7] Lead in the form of tetraethyl lead was added to gasoline in the United States in large amounts from the 1950s until it was banned in the mid-1970s.

[8] 10 to 30 micrograms per 100 milliliters

Sulfur dioxide is a very water-soluble gas and therefore most of the sulfur dioxide that is inhaled is absorbed in the upper respiratory tract and does not reach the lung's airways. However, the small amount of sulfur dioxide that does penetrate into the airways can provoke important health effects, primarily in individuals with asthma.

For those with asthma, even relatively short-term, low-level exposures to sulfur dioxide can result in airway constriction leading to difficulty in breathing and possibly contribute to the severity of an asthmatic attack.

A number of epidemiological studies have shown associations between ambient sulfur dioxide and rates of mortality (death) and morbidity (illness). However, because sulfur dioxide is often strongly correlated with fine particles and especially sulfate-containing particles, it is difficult to separate the effects of sulfur dioxide from those of the particle compounds.

A study in France found an increase of 2.9 visits to the emergency room for every 20 micrograms per cubic meter increase in atmospheric sulfur dioxide. The results pertained to days when the average sulfur dioxide levels were above 68 micrograms per cubic meter but below the U.S. health standard.

In London, asthma and other lower respiratory diseases in children were most significantly associated with exposures to nitrogen dioxide, carbon monoxide, and sulfur dioxide. In adults the only consistent association was with particulate matter.

Hospital admissions for children with asthma may increase by 20 percent following acute exposure to ozone peaks and possibly with sulfur dioxide. Chronic exposure to increased levels of fine particles, sulfur dioxide, and nitrogen dioxide may be associated with up to threefold increase in nonspecific respiratory symptoms. Thus, recent literature suggests that sulfur dioxide affects adults and children differently and that chronic and acute effects may also be different.

Diesel Emissions

Diesel fuel is burned to power buses, trucks, road-building equipment, trains, boats and ships and electricity-generating equipment. When diesel fuel is burned, the exhaust includes both particles and gases. Diesel emissions are important constituents of ambient air pollution.

What's in Diesel?

Diesel particles consist mainly of elemental carbon and other carbon-containing compounds. Hundreds of compounds have been identified as constituents of diesel particles. These include polycyclic aromatic hydrocarbons (PAHs) and other compounds that have been associated with tumor formation and cancer. In 1998, the California Air Resources Board designated diesel particulate a cancer-causing toxic air contaminant.

Diesel particles are microscopic. More than 90 percent of them are less than 1 micron in diameter. Due to their minute size, diesel particles can penetrate deeply into the lung. There is evidence that once in the lung, diesel particles may stay there for a long time.

In addition to particles, diesel exhaust contains several gaseous compounds including carbon monoxide, nitrogen oxides, sulfur dioxide and organic vapors, for example formaldehyde and 1,3-butadiene. Formaldehyde and 1,3-butadiene have been classified as toxic and hazardous air pollutants. Both have been shown to cause tumors in animal studies and there is evidence that exposure to high levels of 1,3-butadiene can cause cancer in humans.

AQMD's recent landmark research project, the Multiple Air Toxics Exposure Study II, found that diesel particulate is responsible for about 70 percent of the total cancer risk from all toxic air pollution in the greater Los Angeles metropolitan area.

Diesel emissions may also be a problem for asthmatics. Some studies suggest that children with asthma who live near roadways with high amounts of diesel truck traffic have more asthma attacks and use more asthma medication.

Some human volunteers, exposed to diesel exhaust in carefully controlled laboratory studies, reported symptoms such as eye and throat irritation, coughing, phlegm production, difficulty breathing, headache, lightheadedness, nausea and perception of unpleasant odors. Another laboratory study, in which volunteers were exposed to relatively high levels of diesel particles for about an hour, showed that such exposures could cause lung inflammation.

Thus current epidemiological and laboratory evidence suggests that at typical urban concentrations, diesel exhaust may contribute significantly to the health effects of air pollution.

What Can Be Done to Reduce the Effects of Air Pollution on Children's Health?

After reviewing the literature on how children's exposures differ from those of adults, it is evident that:

- children are outdoors more hours per day than most adults;
- they exert themselves to a greater degree while they are outside than most adults; and
- they participate in more organized activities than adults.

There are definite health benefits to having children participate in outdoor activities. However, scientific evidence also suggests that air pollution exposures can injure children's lungs and other organs.

Air quality information in the form of health reports and air quality advisories are now a regular part of life in California. One logical step is to reduce strenuous activities during pollution episodes and try to take advantage of those hours when airborne pollutant levels are lower.

At the public level there is a long-standing commitment to improve air quality. When you look at the air pollution levels in California today you can see that a great deal of progress has been made. There has been a cost for this progress. For instance, some products are more expensive. In return, the lower levels of pollutant exposure compared to 20 years ago should decrease the adverse effect of air pollution on the long-term health of our developing children.

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Research Article

Ambient Air Pollution and Atherosclerosis in Los Angeles

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Abstract
Associations have been found between long-term exposure to ambient air pollution and cardiovascular morbidity and mortality. The contribution of air pollution to atherosclerosis that underlies many cardiovascular diseases has not been investigated. Animal data suggest that ambient particulate matter (PM) may contribute to atherogenesis. We used data on 798 participants from two clinical trials to investigate the association between atherosclerosis and long-term exposure to ambient PM up to 2.5 μm in aerodynamic diameter ($PM_{2.5}$). Baseline data included assessment of the carotid intima-media thickness (CIMT), a measure of subclinical atherosclerosis. We geocoded subjects' residential areas to assign annual mean concentrations of ambient $PM_{2.5}$. Exposure values were assigned from a $PM_{2.5}$ surface derived from a geostatistical model. Individually assigned annual mean $PM_{2.5}$ concentrations ranged from 5.2 to 26.9 $\mu g/m^3$ (mean, 20.3). For a cross-sectional exposure contrast of 10 $\mu g/m^3$ $PM_{2.5}$, CIMT increased by 5.9% (95% confidence interval, 1-11%). Adjustment for age reduced the coefficients, but further adjustment for covariates indicated robust estimates in the range of 3.9-4.3% (*p*-values, 0.05-0.1). Among older subjects (≥ 60 years of age), women, never smokers, and those reporting lipid-lowering treatment at baseline, the associations of $PM_{2.5}$ and CIMT were larger with the strongest associations in women ≥ 60 years of age (15.7%, 5.7-26.6%). These results represent the first epidemiologic evidence of an association between atherosclerosis and ambient air pollution. Given the leading role of cardiovascular disease as a cause of death and the large populations exposed to ambient $PM_{2.5}$, these findings may be important and need further confirmation. *Key words:* air pollution, atherosclerosis, particulate matter. *Environ Health Perspect* 113:201-206 (2005). doi:10.1289/ehp.7523 available via http://dx.doi.org/ [Online 22 November 2004]

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Introduction

A large body of epidemiologic evidence suggests associations between ambient air pollution and cardiovascular mortality and morbidity (Peters and Pope 2002; Pope et al. 2004). All of these studies focus on events occurring at a late stage of vascular disease processes. The impact of air pollution on the underlying preclinical conditions remains poorly understood.

We hypothesize that current levels of ambient particulate matter (PM) up to 2.5 μm in aerodynamic diameter ($PM_{2.5}$) may contribute to atherosclerosis, leading to subclinical anatomical changes that play a major role in cardiovascular morbidity and mortality later in life. Animal studies support our hypothesis by showing that inhalation of ambient PM promotes oxidative lung damage, including alveolar and systemic inflammatory responses (Becker et al. 1996; Dye et al. 2001; Fujii et al. 2002; Goto et al. 2004; Suwa et al. 2002; van Eeden et al. 2001).

We investigated the association between residential ambient $PM_{2.5}$ and carotid artery intima-media thickness (CIMT) using prerandomization baseline data from two recent clinical trials conducted in Los Angeles, California (Hodis et al. 2002). CIMT is a well-established quantitative measure of generalized atherosclerosis that correlates well with all of the major cardiovascular risk factors, with coronary artery atherosclerosis, and with clinical cardiovascular events (Mack et al. 2000). It is an established tool for investigating the contribution of long-term exposures such as smoking or passive smoking to subclinical stages of atherosclerosis at any given age (Diez-Roux et al. 1995; Howard et al. 1994, 1998). This is the first study to assess the association of atherosclerosis with air pollution.

Materials and Methods

Population and health assessment. We used baseline health data from two randomized, double-blind, placebo-controlled clinical trials conducted at the University of Southern California Atherosclerosis Research Unit (Hodis et al. 2002). The Vitamin E Atherosclerosis Progression Study (VEAPS) investigated the effects of vitamin E on the progression of atherosclerosis measured by CIMT. The B-Vitamin Atherosclerosis Intervention Trial (BVAIT) focused on the effect of vitamin B supplements on the progression of atherosclerosis (trial in progress). Baseline assessment in both trials included CIMT measured between 1998 and 2003 using the same standardized methods (Hodis et al. 2002; Selzer et al. 1994, 2001). Recruitment of volunteers occurred over the entire Los Angeles Basin, covering a geographic area of approximately 64,000 km^2.

Eligible subjects for the VEAPS trial (n = 353) were men and women ≥ 40 years of age with slightly increased LDL cholesterol (≥ 3.37 mmol/L) but with no clinical signs or symptoms of cardiovascular disease (CVD) (Hodis et al. 2002). Subjects with diabetes, diastolic blood pressure > 100 mm Hg, thyroid disease, serum creatinine > 0.065 mmol/L, life-threatening diseases, or high alcohol intake were excluded.

BVAIT (n = 506) had a similar design to that of VEAPS. Men and women > 40 years of age were prescreened to meet study criteria (fasting plasma homocysteine ≥ 8.5 μmol/L; postmenopausal for women; no evidence of diabetes, heart disease, stroke, or cancer). Subjects were excluded on the basis of any clinical signs or symptoms of CVD, diabetes or fasting serum glucose ≥ 140 mg/dL, triglyceride levels ≥ 150 mg/dL, serum creatinine > 1.6 mg/dL, high blood pressure, untreated thyroid disease, life-threatening disease with prognosis < 5 years, or high alcohol intake.

Thus, our study included "healthy" subjects with biomarkers (elevated LDL cholesterol or homocysteine) that suggested an increased risk of future CVDs (n = 859). Fifty-eight subjects were excluded in the exposure assignment process because they lived outside the area with $PM_{2.5}$ data. Three subjects had missing data in at least one of the covariates used in the models. Our total sample consisted of 798 participants.

Health measures, including CIMT. Our main outcome of interest is CIMT. In both trials, high-resolution B-mode ultrasound images of the right common carotid artery were obtained before the intervention (baseline) with a 7.5-MHz linear array transducer attached to an ATL Ultramark-4 Plus Ultrasound System (Ultramark, Bothell, WA). We used this baseline CIMT measurement as the outcome. Details of this highly reproducible method are published (Hodis et al. 2002; Selzer et al. 1994, 2001). Blood pressure, height, and weight were measured with standard procedures.

The baseline questionnaires included an assessment of all major CVD risk factors and covariates, including clinical events, diet, use of prescription medications, physical activity, current and past smoking and passive smoking, and vitamin supplements. Age, education, and other sociodemographic factors were available for each subject. Fasting blood samples were also drawn for lipid measurements. Data used in our analyses were collected with the same tools in both trials.

Exposure assignment. To assess exposure we chose a novel approach derived from a geographic information system (GIS) and geostatistics. This method allows for assignment of long-term mean ambient concentrations of $PM_{2.5}$ to the ZIP code area of each subject's residential address (Künzli and Tager 2000). The resulting surface of $PM_{2.5}$ covered the entire Los Angeles metropolitan area. The surface is derived from a geostatistical model and data from 23 state and local district monitoring stations (during 2000). These monitors are located across the Los Angeles region to characterize urban levels of pollution. To assign exposure, $PM_{2.5}$ data were interpolated using a combination of a universal kriging model

with a quadratic drift and a multiquadric radial basis function model (Bailey and Gatrell 1995; Burrough and McDonnell 1998). We averaged the two surfaces based on 25-m grid cells. Examination of errors from the universal model showed that > 50% of the study area had assigned values within 15% of monitored concentrations, whereas 67% were within 20%. The larger errors were on the periphery of our study area, where the density of study participants was the lowest. We linked the ZIP code centroids of each subject with the exposure surface through a geocoding database [Environmental Systems Research Institute (ESRI) 2004]. Figure 1 illustrates the $PM_{2.5}$ surface with the geolocated ZIP codes. Individually assigned $PM_{2.5}$ data had a range from 5.2 to 26.9 $\mu g/m^3$ (mean, 20.3), thus exceeding the range observed across 156 metropolitan areas used in the largest cohort study of air pollution and mortality (Pope et al. 2002). All models were implemented with ArcScript from ESRI (Redlands, CA).

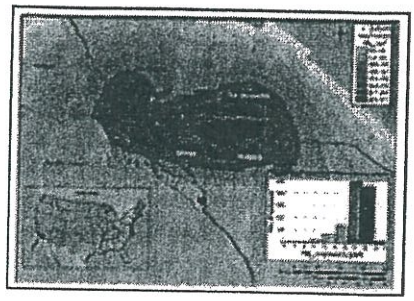


Figure 1. ZIP code locations of the study population geocoded on the $PM_{2.5}$ surface, modeled with 2000 $PM_{2.5}$ data, and distribution of individually assigned concentrations.

Statistical analyses. We tested the univariate and multivariate associations between CIMT and ambient $PM_{2.5}$ using linear regression analyses. Extensive residual diagnostics indicated some heteroskedasticity, which was rectified with the natural log-transformed CIMT. We adjusted for factors that were statistically associated with both CIMT and ambient $PM_{2.5}$ (age, male sex, low education, and low income). Next, we expanded the models using covariates that were associated with either $PM_{2.5}$ or CIMT, including indicator variables for current second-hand smoke exposure and current and former personal smoking. We then added covariates that play a role in atherosclerosis such as blood pressure, LDL cholesterol, or proxy measures such as reporting treatment with antihypertensives or lipid-lowering medications at study entry. These factors may affect the pathophysiologic pathways linking air pollution exposure and atherosclerosis (Ross 1999); thus, such models may overadjust the coefficients. We chose this conservative approach to test the sensitivity of the effect estimates under a broad range of model assumptions.

There is increasing evidence that host factors such as age, sex, or underlying disease and risk profiles may modify the effects of air pollution (Pope et al. 2002; Zanobetti and Schwartz 2002). Furthermore, the finding of atherosclerosis in PM-exposed rabbits was based on a hyperlipidemic trait (Suwa et al. 2002). Therefore, we also stratified by sex, age (< 60 years, ≥ 60 years), smoking status, and lipid-lowering drug therapy.

Results

Table 1 summarizes the main characteristics of the study population and among main subgroups. Table 2 presents the percent change in CIMT in association with a 10 $\mu g/m^3$ contrast in ambient $PM_{2.5}$ concentrations for three cross-sectional regression models. The unadjusted model indicates a 5.9% [95% confidence interval (CI), 1-11%] increase in CIMT per 10 $\mu g/m^3$ $PM_{2.5}$. For the observed contrast between lowest and highest exposure (20 $\mu g/m^3$ $PM_{2.5}$), this corresponds to a 12.1% (2.0-23.1%) increase in CIMT. The only covariate with a substantial effect on the point estimate was age, which reduced the effect from 5.9 to 4.3% (0.4-9%) per 10 $\mu g/m^3$ $PM_{2.5}$. This change agrees with the age-related effect modification. Otherwise, effect estimates across the models remained robust, in the range of 3.9-4.3% with *p*-values from 0.05 to 0.1. To corroborate the exposure-response relationship, we also categorized $PM_{2.5}$ levels into quartiles. Figure 2 shows the adjusted mean CIMT across these four groups of equal sample size at the mean levels of the covariates (age, sex, education, and income). The trend across the exposure groups was statistically significant ($p = 0.041$). The unadjusted means of CIMT among these quartiles of exposure were 734, 753, 758, and 774 µm, respectively.

Table 1.

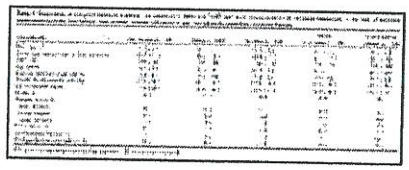
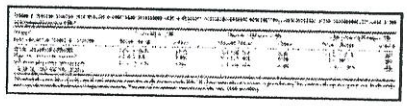
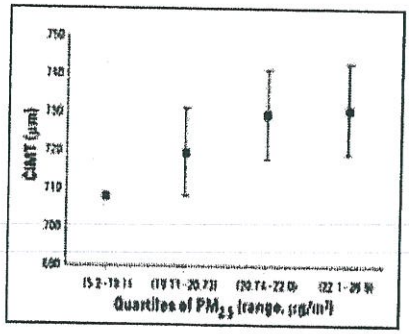


Table 2.





The associations between CIMT and $PM_{2.5}$ were substantially stronger among 109 subjects reporting lipid-lowering medication at study entry, both in men and in women (Table 2, Figure 3). The crude effect reached 15.8% (2-31%) per 10 $\mu g/m^3$ $PM_{2.5}$, with adjusted values ranging between 12 and 16%. Despite the small sample size, *p*-values of all models were mostly < 0.1 and often < 0.05.

Results also suggest significant age and sex interactions, with much larger effects in women and in the older age group (Figure 3). Effect estimates in

women were statistically significant and typically in the range of 6-9% per 10 $\mu g/m^3$ $PM_{2.5}$. Associations were strongest among women $\geq$ 60 years of age (n = 186), leading to crude estimates of 19.2% (9-31%). Adjusted coefficients ranged from 14 to 19%, being statistically significant in all models and sensitivity analyses.

Among never smokers (n = 502), the effect estimate reached 6.6% (1.0-12.3%). The estimate was small and not significant in current (n = 30) and former smokers (n = 265).

Figure 2. Mean CIMT ± 1 SE among quartiles of the $PM_{2.5}$ distribution. The *y*-axis shows mean CIMT levels at the population average of the adjustment covariates (age, sex, education, and income). The first quartile is the reference group.

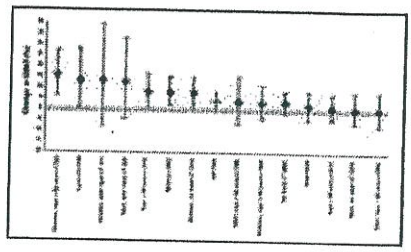


Figure 3. Percent difference and 95% CI in CIMT associated with a 10 $\mu g/m^3$ contrast in ambient $PM_{2.5}$ in all subjects and in subgroups. Lipid-LT, lipid-lowering therapy. All estimates are based on the cross-sectional linear model with log intima-media thickness as the dependent variable and home outdoor $PM_{2.5}$ as the independent variable, adjusted for sex, age, education, and income. Numbers in parentheses are numbers of subjects per group. Data are ordered by size of point estimate; the null effect line is indicated by a dash.

Discussion

Our study presents the first evidence for an association between CIMT and long-term exposure to ambient air pollution. As recently reviewed in a statement of the American Heart Association (Brook et al. 2004) substantial epidemiologic and experimental evidence suggests a contribution of ambient air pollutants on cardiovascular mortality and morbidity. However, these studies focus on acute and subacute effects on cardiac autonomic function, inflammatory or thrombogenic markers, arrhythmia, myocardial infarction, cardiovascular hospital admission, and death. The only outcome considered in long-term air pollution studies has been mortality. The relative risks for acute effects on mortality have been substantially smaller than those observed for long-term associations (Pope et al. 2002; Samet et al. 2000). As shown previously, cohort studies are capable of capturing acute and chronic effects of air pollution on the course of diseases that ultimately lead to premature death (Künzli et al. 2001). In contrast, time-series and panel studies investigate only the associations of event occurrence with the most recent exposure (Künzli et al. 2001). Thus, if air pollution has both acute and cumulative long-term effects, one expects larger mortality coefficients in cohort studies. CIMT reflects long-term past exposure; thus, we provide the first evidence for chronic effects of air pollution on atherogenesis that may in part explain the above mentioned discrepancy between acute and long-term risk estimates (Pope et al. 2002; Samet et al. 2000).

There are several major aspects to be considered in the interpretation of this new finding, mainly the strength in the exposure assignment, the limited evidence for bias, the differences in effects within subgroups, and plausibility.

Exposure assignment. The individual residence-based assignment of exposure represents a substantial improvement over most studies that have relied on central monitors or on binary road buffers combined with basic interpolation (Hoek et al. 2002; Pope et al. 2004). As a sensitivity analysis, we used weighted least-squares models with the weights specified as the inverse of the standard errors from the universal kriging model to down-weight estimates with larger error. In addition, we implemented models based solely on the universal kriging estimate. In both instances results were robust and similar to what we found with our main model.

Time-activity studies show that people spend most of their time in or around home, and our restriction of exposure assessment on residential address captures the most relevant part of exposure (Leech et al. 2002). $PM_{2.5}$ generally displays spatially homogeneous distributions across small areas such as neighborhoods and blocks, and as a result, the ambient conditions at the ZIP code centroid likely reflect the levels expected at home outdoors (Roosli et al. 2000). $PM_{2.5}$ of outdoor origin will also penetrate indoors, and correlations between long-term outdoor PM concentrations and indoor levels of PM from outdoor origin is high (Sarnat et al. 2000). Exposure to ambient air pollution while working and during commute are not included in our exposure term but are considered to be a relevant source of exposure (Riediker et al. 2003). Although most likely a random misclassification with biases toward the null, the errors may affect subgroups differently, thus explaining part of the observed interactions.

In Los Angeles, no clear trends have been observed in $PM_{2.5}$ concentrations over the past 5-10 years. The year 2000 surface characterizes the prevailing mean $PM_{2.5}$ concentrations across several years and can be considered a measure of long-term past exposure. This year also sits in the middle of the baseline recruitment period. Overall, the various limitations in our exposure assignment may add some random error, biasing results toward weaker associations (Thomas et al. 1993).

We also assigned ambient ozone to ZIP code centroids. Inclusion of ozone in the models had no impact on the $PM_{2.5}$ coefficients or the SEs. Ozone and $PM_{2.5}$ were not correlated (r = -0.17), and the $PM_{2.5}$ estimates were not substantially

different in low- and high-ozone regions. The estimates of association for ozone were positive but not statistically significant and much smaller than for $PM_{2.5}$. This finding must be put in context of the specific challenges in determining long-term exposure to ozone, which are substantially different than in the case of PM exposure. In contrast to $PM_{2.5}$ from outdoor origin, ambient ozone levels have lower correlations with personal exposure (Avol et al. 1998; Sarnat et al. 2000, 2002); therefore, the ability to detect effects of ozone will likely be reduced due to greater misclassification.

Biases. Our subjects were a nonrandom sample of "healthy" volunteers with above-average education, meeting strict inclusion criteria for the two clinical trials. Although we cannot exclude some systematic selection biases affecting the cross-sectional data, it is unlikely that subjects with preclinical signs of atherosclerosis would have been more likely to volunteer if they lived in more polluted areas. Although the selection of subjects limits the generalization to other populations, we do not expect this to lead to over- or underestimating the cross-sectional associations. The two trials recruited subjects independently; thus, the effects may be compared across trials to evaluate the potential influence of selecting volunteers. The populations differed with regard to age, smoking habits, baseline LDL and treatment, blood pressure, active and passive smoking, and other relevant factors; thus, the $PM_{2.5}$ coefficients were smaller and were not statistically significant in the VEAPS trial with its younger population. However, after taking these factors into account, the associations with ambient $PM_{2.5}$ were similar. For example, among elderly women of VEAPS (n = 70) and BVAIT (n = 116), the effect estimate was 18.1% (-0.1 to 36.3.%) and 13.6% (2.8-24.4.%), respectively. There is some evidence for larger effects in subjects with cardiovascular risk factors, indicated by prescriptions of lipid-lowering treatment. Our trials excluded subjects with clinically manifest CVDs. Moreover, if air pollution amplifies systemic inflammation among those prone to atherosclerosis, exclusion of subjects with high LDL may be a source of bias. One may expect effect estimates in a less selected, less healthy population to be larger than those reported.

The wealth of baseline data from these clinical trials offered the opportunity to control for a broad array of covariates. Apart from the effect of age adjustment, estimates were robust to numerous combinations of covariates, including income, education, active and passive tobacco smoke, cardiovascular prescriptions, vitamin intake, and physical activity. Uncontrolled or residual confounding appears to be an unlikely explanation for these results. Among women, adjustment for hormone replacement therapies did not affect the $PM_{2.5}$ estimates.

In previous studies, we found that spatial autocorrelation in the residuals could affect the size and significance of pollution coefficients (Jerrett et al. 2003a). We investigated spatial autocorrelation of the unstandardized residuals. We assessed autocorrelation with first-order, adjusted first-order, and second-order spatial weight matrices based on nearest neighbor contiguity, but we found no evidence of spatial autocorrelation. This supports the conclusion that the models supply efficient unbiased estimates (Jerrett et al. 2003b). As part of our sensitivity analyses, we also derived $PM_{2.5}$ surfaces using different interpolations and weighted least squares with weights equal to the inverse of the standard error of the exposure estimate. All approaches produced very similar results.

Evidence for effect modification. The data suggest substantial interactions with age, sex, smoking, and underlying cardiovascular risk factors. Given the reduced sample size among subgroups, the recruitment of volunteers, and the cross-sectional nature of the data, it is difficult to fully explore the causes of the observed modifications of associations and to establish susceptibility profiles. If the exposure misclassifications differed across subgroups, part of the interactions may be explained by differential exposure error. The sex and age difference could also be an artifact due to measurement error in the assigned exposure because time spent in commuting and location of work places may be different in men and women and in the young and elderly. Empirical studies on mobility suggest women have smaller activity spaces than men and younger groups, meaning they tend to spend more time in and around the home (Kwan and Lee 2004), and the same is probably true of the elderly compared with younger groups. Exposure measurement error may be reduced in those spending more time at home, leading to stronger effects (Thomas et al. 1993). Moreover, differences in statistical power may play a role as well; as shown at least for the 25-40-year age range, power to detect effects on CIMT is larger in women than in men (Stein et al. 2004).

The finding that those reporting prescriptions of lipid-lowering medications at baseline showed stronger associations of CIMT with $PM_{2.5}$ merits further investigation. This result agrees with the observed effects of PM on atherosclerosis in experiments conducted in hyperlipidemic rabbits (Goto et al. 2004; Suwa et al. 2002). The systemic inflammatory and atherogenic reaction in these rabbits was related to the amount of PM contained in the alveolar macrophages. In our study, being under lipid-lowering therapy is an indicator for risk profiles prone to atherogenesis. Those subjects were mostly men (64%) and, on average, older, more often active or passive smokers, and almost twice as likely to report antihypertensive treatment. The systemic response to ambient PM may amplify and expand the oxidation of LDL cholesterol among these susceptible subjects, consequently contributing to injury in the artery wall (Goto et al. 2004; Ross 1999). Investigations of short-term effects of ambient air pollution on mortality also suggest that underlying risk profiles such as diabetes may amplify susceptibility to ambient PM (Zanobetti and Schwartz 2002), and similar findings have been shown with smoking and diabetes mellitus in association with CIMT (Karim et al. 2005). To clarify the relevance of lipid status, it would be interesting to investigate our hypothesis among cohorts with familial hypercholesteremia (Wiegman et al. 2004; Wittekoek et al. 1999).

As shown in Figure 3, the size of the point estimate was larger among the older subjects. Future research needs to clarify whether air pollution contributes to atherosclerosis only after a certain age or early on. Effects of air pollution on lung development have been observed during adolescence and may be a result of both pulmonary and chronic systemic inflammatory effects (Gauderman et al. 2002); thus, it is conceivable that atherogenic responses may occur early in life. The age dependence of the effects may also be codetermined by genetic factors (Humphries and Morgan 2004; Ross 1999).

We also observed larger effects in women. If other cardiovascular risk factors such as occupational exposures dominate atherosclerosis in men, we would expect a smaller effect signal and less precision in the estimates among men. We also hypothesize that interactions may reflect biologic causes. If premenopausal women are protected against atherosclerosis by endogenous hormones, loss of hormonal protection would lead to increased vulnerability after menopause (Kannel et al. 1976). This could explain part of the interaction by both age and sex.

Active and passive smoking did not confound results in either the total sample or among subgroups. Adjustment for active tobacco smoke led to a slight increase in the effect estimate; thus, residual confounding is unlikely to overestimate the effects. However, $PM_{2.5}$ associations were clearly stronger in never smokers compared with smokers (data not shown). This gradient was also observed in all subgroups with significant $PM_{2.5}$ associations (Figure 3). Oxidative and inflammatory effects of smoking may dominate to such an extent that the additional exposure to ambient air pollutants may not further enhance effects along the same pathways. The difference in the effects of $PM_{2.5}$ in smokers and nonsmokers needs further investigation. The American Cancer Society cohort study does not reveal a clear pattern of a smoking interaction for the association of ambient air pollution and cardiovascular death (Krewski et al. 2004; Pope et al. 2004). In the Study on Air Pollution and Lung Diseases in Adults (SAPALDIA), associations between air pollution and level of pulmonary function did not differ by smoking status (Ackermann-Liebrich et al. 1997).

Some U.S. studies indicate effect modification of air pollution by socioeconomic status (SES) with much stronger effects among the less educated (Pope et al. 2002). The cause of this interaction pattern is not well understood. SES status was rather homogeneous in these mostly well-educated volunteers, providing little power to investigate interactions of pollution with SES. If lower SES also positively modifies effects of air pollution on atherosclerosis, our population would provide an underestimate of the health effects in the general population (O'Neill et al. 2003). Further research on samples representative of the population will be needed to assess whether the high SES in the clinical trials biases the effects toward the null.

Future research should focus on identifying factors that determine susceptibility to $PM_{2.5}$. We are initiating studies on subjects with inflammatory metabolic syndromes prone to accelerated atherosclerosis such as postmenopausal women, diabetics, or obese or physically inactive people. To corroborate the cross-sectional findings, follow-up studies are ultimately needed to investigate the association of concurrent levels of air pollution exposure with the progression of CIMT.

Plausibility. From a biologic perspective, our results support the hypothesis that long-term exposure to ambient PM contributes to systemic inflammatory pathways, which are a relevant aspect of atherogenesis (Ross 1999). The findings indicate a biologically plausible link between the observed acute effects of ambient air pollution on systemic inflammation (Glantz 2002) and the long-term consequences of sustained vascular inflammation leading to increased atherosclerosis and, ultimately, cardiovascular death (Hoek et al. 2002; Pope et al. 2004). Among susceptible people, this may lead to artery wall lesions similar to those observed in the rabbit model (Fujii et al. 2002; Suwa et al. 2002). In these hyperlipidemic rabbits, 4-week PM exposure was associated with the progression of atherosclerotic lesions, coupled with an enhanced release of bone marrow monocytes. These precursors of macrophages play an important role in the atherogenic inflammatory responses (Goto et al. 2004; Ross 1999; Suwa et al. 2002). Given the central role of oxidized LDL in the initiation and progression of atherogenesis, suggestions that the plasma of automotive workers with high exposure to traffic exhaust is more susceptible to oxidation is also of interest (Sharman et al. 2002).

As a quantitative plausibility check, we compared the size of the $PM_{2.5}$ effects with effects of other risk factors on CIMT. Using smoking and environmental tobacco smoke (ETS) as a model for air pollution exposure, the size of our estimates appear plausible (Diez-Roux et al. 1995; Howard et al. 1994). Associations of ETS and current levels of air pollution with various respiratory outcomes are similar and support the notion of common underlying pathways (Künzli 2002). Smoking and ETS associate with stiffer and thicker artery walls, reflecting the systemic effect of these exposures (Howard et al. 1994; Mack et al. 2003). Exposure to ETS was associated with 2-3% thicker intima-media, which approximate the effects observed for a 10 $\mu g/m^3$ change in $PM_{2.5}$ (Diez-Roux et al. 1995; Howard et al. 1994). Using never smokers without ETS exposure as the referent group in our data, never smokers with ETS at home had 0.9% (-2.7 to 4.5%) thicker artery walls; former smokers' CIMT was increased on average by 3.4% (0.7-6.3%), and the 30 current smokers had 5% (-1.5 to 11.6%) thicker CIMT. The trend across these four categories of tobacco exposure was statistically significant. As shown in Table 1, smokers were underrepresented in these volunteers of well-educated participants.

The observed percent change in CIMT corresponds to an increase in the thickness of approximately 20-40 μm per 10

$\mu g/m^3$ contrast in $PM_{2.5}$. This difference in CIMT translates into some 3-6% increase in the long-term risk for myocardial infarction (O'Leary et al. 1999). Pope et al. (2004) reported that long-term exposure to $PM_{2.5}$ was associated with an 18% (14-23%) increase in ischemic heart disease. Effect sizes reported here concur with these findings, indicating that a fraction of the total effect of ambient PM on cardiovascular mortality may be mediated through sustained long-term effects of air pollution on atherosclerosis (Künzli et al. 2001). This is in line with the proposed model (Künzli et al. 2001) in which some of the effects observed in cohort studies must reflect long-term contributions of air pollution to the underlying disease progression, whereas in other cases, air pollution contributes only to triggering of cardiovascular events or death (Bell et al. 2004; Künzli et al. 2001; Peters and Pope 2002).

From a biologic and policy perspective, we emphasize that $PM_{2.5}$ probably serves as a surrogate for the mixture of urban air pollution and constituents of PM. It is premature to conclude that $PM_{2.5}$ and its constituents are the atherogenic culprit per se. Atherosclerosis results from complex processes that may include a combination of various urban pollutants, host factors, and pathways that ultimately lead to the findings of a CIMT-$PM_{2.5}$ association.

In conclusion, we have presented the first epidemiologic evidence supporting the idea of a chronic vascular response to respiratory and systemic effects of PM exposure. Given the leading role of heart disease as a cause of death in most westernized countries and the growing contribution in developing countries, these findings may be of high public health relevance. Further investigations need to focus on susceptible groups and follow-up of cohorts to investigate the effect of air pollution on the progression of CIMT.

References

Ackermann-Liebrich U, Leuenberger P, Schwartz J, Schindler C, Monn C, Bolognini G, et al. 1997. Lung function and long term exposure to air pollutants in Switzerland. Study on Air Pollution and Lung Diseases in Adults (SAPALDIA) Team. Am J Respir Crit Care Med 155(1): 122-129.

Avol EL, Navidi WC, Colome SD. 1998. Modeling ozone levels in and around Southern California homes. Environ Sci Technol 32:463-468.

Bailey T, Gatrell A. 1995. Interactive Spatial Data Analysis. New York:Longman.

Becker S, Soukup JM, Gilmour MI, Devlin RB. 1996. Stimulation of human and rat alveolar macrophages by urban air particulates: effects on oxidant radical generation and cytokine production. Toxicol Appl Pharmacol 141(2): 637-648.

Bell ML, Samet JM, Dominici F. 2004. Time-series studies of particulate matter. Annu Rev Public Health 25:247-280.

Brook RD, Franklin B, Cascio W, Hong Y, Howard G, Lipsett M, et al. 2004. Air pollution and cardiovascular disease: a statement for healthcare professionals from the Expert Panel on Population and Prevention Science of the American Heart Association. Circulation 109(21):2655-2671.

Burrough P, McDonnell R. 1998. Principles of Geographical Information Systems. New York:Oxford University Press.

Diez-Roux AV, Nieto FJ, Comstock GW, Howard G, Szklo M. 1995. The relationship of active and passive smoking to carotid atherosclerosis 12-14 years later. Prev Med 24(1):48-55.

Dye JA, Lehmann JR, McGee JK, Winsett DW, Ledbetter AD, Everitt JI, et al. 2001. Acute pulmonary toxicity of particulate matter filter extracts in rats: coherence with epidemiologic studies in Utah Valley residents. Environ Health Perspect 109(suppl 3):395-403.

ESRI. 2004. ArcGIS. Redlands, CA: Environmental Systems Research Institute. Available: http://www.esri.com/software/arcgis/index.html [accessed 29 December 2004].

Fujii T, Hayashi S, Hogg JC, Mukae H, Suwa T, Goto Y, et al. 2002. Interaction of alveolar macrophages and airway epithelial cells following exposure to particulate matter produces mediators that stimulate the bone marrow. Am J Respir Cell Mol Biol 27(1):34-41.

Gauderman WJ, Gilliland GF, Vora H, Avol E, Stram D, McConnell R, et al. 2002. Association between air pollution and lung function growth in Southern California children: results from a second cohort. Am J Respir Crit Care Med 166(1):76-84.

Glantz SA. 2002. Air pollution as a cause of heart disease. Time for action. J Am Coll Cardiol 39(6): 943-945.

Goto Y, Hogg JC, Shih CH, Ishii H, Vincent R, van Eeden SF. 2004. Exposure to ambient particles accelerates monocyte release from the bone marrow in atherosclerotic rabbits. Am J Physiol Lung Cell Mol Physiol 287: L79-85.

Hodis HN, Mack WJ, LaBree L, Mahrer PR, Sevanian A, Liu CR, et al. 2002. Alpha-tocopherol supplementation in healthy individuals reduces low-density lipoprotein oxidation but not atherosclerosis: the Vitamin E Atherosclerosis Prevention Study (VEAPS). Circulation 106(12): 1453-1459.

Hoek G, Brunekreef B, Goldbohm S, Fischer P, van den Brandt PA. 2002. Association between mortality and indicators of traffic-related air pollution in the

Netherlands: a cohort study. Lancet 360(9341):1203-1209.

Howard G, Burke GL, Szklo M, Tell GS, Eckfeldt J, Evans G, et al. 1994. Active and passive smoking are associated with increased carotid wall thickness. The Atherosclerosis Risk in Communities Study. Arch Intern Med 154(11):1277-1282.

Howard G, Wagenknecht LE, Burke GL, Diez-Roux A, Evans GW, McGovern P, et al. 1998. Cigarette smoking and progression of atherosclerosis: the Atherosclerosis Risk in Communities (ARIC) Study. JAMA 279(2):119-124.

Humphries SE, Morgan L. 2004. Genetic risk factors for stroke and carotid atherosclerosis: insights into pathophysiology from candidate gene approaches. Lancet Neurol 3(4):227-235.

Jerrett M, Burnett R, Goldberg M, Sears M, Krewski D, Catalan R, et al. 2003a. Spatial analysis for environmental health research: concepts, methods, and examples. J Toxicol Environ Health A 66(16-19):1783-1810.

Jerrett M, Burnett RT, Willis A, Krewski D, Goldberg MS, DeLuca P, et al. 2003b. Spatial analysis of the air pollution-mortality relationship in the context of ecologic confounders. J Toxicol Environ Health A 66(16-19): 1735-1777.

Kannel WB, Hjortland MC, McNamara PM, Gordon T. 1976. Menopause and risk of cardiovascular disease: the Framingham study. Ann Intern Med 85(4):447-452.

Karim R, Buchanan TA, Hodis HN, Li Y, Mack WJ. 2005. The association of smoking and subclinical atherosclerosis in type 2 diabetes: modification by duration of diabetes. Diabet Med 22(1):81-87.

Krewski D, Burnett RT, Goldberg MS, Hoover K, Siemiatycki J, Abrahamowicz M, et al. 2004. Validation of the Harvard Six Cities Study of particulate air pollution and mortality. N Engl J Med 350(2):198-199.

Künzli N. 2002. The public health relevance of air pollution abatement. Eur Respir J 20(1): 198-209.

Künzli N, Medina S, Kaiser R, Quenel P, Horak FJ, Studnicka M. 2001. Assessment of deaths attributable to air pollution: should we use risk estimates based on time series or on cohort studies? Am J Epidemiol 153(11):1050-1055.

Künzli N, Tager I. 2000. Long-term health effects of particulate and other ambient air pollution: research can progress faster if we want it to. Environ Health Perspect 108:915-918.

Kwan MP, Lee J. 2004. Geovisualization of human activity patterns using 3D GIS: a time-geographic approach. In: Spatially Integrated Social Science: Examples in Best Practice (Goodchild MF, Janelle DG, eds). New York:Oxford University Press, 48-66.

Leech JA, Nelson WC, Burnett RT, Aaron S, Raizenne ME. 2002. It's about time: a comparison of Canadian and American time-activity patterns. J Expo Anal Environ Epidemiol 12(6):427-432.

Mack WJ, Islam T, Lee Z, Selzer RH, Hodis HN. 2003. Environmental tobacco smoke and carotid arterial stiffness. Prev Med 37(2):148-154.

Mack WJ, LaBree L, Liu C, Selzer RH, Hodis HN. 2000. Correlations between measures of atherosclerosis change using carotid ultrasonography and coronary angiography. Atherosclerosis 150(2):371-379.

O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK Jr. 1999. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. N Engl J Med 340(1): 14-22.

O'Neill MS, Jerrett M, Kawachi I, Levy JI, Cohen AJ, Gouveia N, et al. 2003. Health, wealth, and air pollution: advancing theory and methods. Environ Health Perspect 111:1861-1870.

Peters A, Pope CA. 2002. Cardiopulmonary mortality and air pollution. Lancet 360(9341):1184-1185.

Pope CA, Burnett RT, Thun MJ, Calle EE, Krewski D, Ito K, et al. 2002. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. JAMA 287(9):1132-1141.

Pope CA, Burnett RT, Thurston GD, Thun MJ, Calle EE, Krewski D, et al. 2004. Cardiovascular mortality and long-term exposure to particulate air pollution: epidemiological evidence of general pathophysiological pathways of disease. Circulation 109(1):71-77.

Riediker M, Williams R, Devlin R, Griggs T, Bromberg P. 2003. Exposure to particulate matter, volatile organic compounds, and other air pollutants inside patrol cars. Environ Sci Technol 37(10):2084-2093.

Roosli M, Braun-Fahrlander C, Künzli N, Oglesby L, Theis G, Camenzind M, et al. 2000. Spatial variability of different fractions of particulate matter within an urban environment and between urban and rural sites. J Air Waste Manag Assoc 50(7):1115-1124.

Ross R. 1999. Atherosclerosis--an inflammatory disease. N Engl J Med 340(2):115-126.

Samet JM, Dominici F, Curriero FC, Coursac I, Zeger SL. 2000. Fine particulate air pollution and mortality in 20 U.S. cities, 1987-1994. N Engl J Med 343(24): 1742-1749.

Sarnat J, Koutrakis P, Suh H. 2000. Assessing the relationship between personal particulate and gaseous exposures of senior citizens living in Baltimore, MD. J Air Waste Manag Assoc 50(7):1184-1198.

Sarnat JA, Long CM, Koutrakis P, Coull BA, Schwartz J, Suh HH. 2002. Using sulfur as a tracer of outdoor fine particulate matter. Environ Sci Technol 36(24): 5305-5314.

Selzer RH, Hodis HN, Kwong-Fu H, Mack WJ, Lee PL, Liu CR, et al. 1994. Evaluation of computerized edge tracking for quantifying intima-media thickness of the common carotid artery from B-mode ultrasound images. Atherosclerosis 111(1):1-11.

Selzer RH, Mack WJ, Lee PL, Kwong-Fu H, Hodis HN. 2001. Improved common carotid elasticity and intima-media thickness measurements from computer analysis of sequential ultrasound frames. Atherosclerosis 154(1): 185-193.

Sharman JE, Coombes JS, Geraghty DP, Fraser DI. 2002. Exposure to automotive pollution increases plasma susceptibility to oxidation. Arch Environ Health 57(6): 536-540.

Stein JH, Douglas PS, Srinivasan SR, Bond MG, Tang R, Li S, et al. 2004. Distribution and cross-sectional age-related increases of carotid artery intima-media thickness in young adults. The Bogalusa Heart Study. Stroke 35: 2782-2787.

Suwa T, Hogg JC, Quinlan KB, Ohgami A, Vincent R, van Eeden SF. 2002. Particulate air pollution induces progression of atherosclerosis. J Am Coll Cardiol 39(6): 935-942.

Thomas D, Stram D, Dwyer J. 1993. Exposure measurement error: influence on exposure-disease relationships and methods of correction. Annu Rev Publ Health 14:69-93.

van Eeden SF, Tan WC, Suwa T, Mukae H, Terashima T, Fujii T, et al. 2001. Cytokines involved in the systemic inflammatory response induced by exposure to particulate matter air pollutants (PM_{10}). Am J Respir Crit Care Med 164(5):826-830.

Wiegman A, Hutten BA, de Groot E, Rodenburg J, Bakker HD, Buller HR, et al. 2004. Efficacy and safety of statin therapy in children with familial hypercholesterolemia: a randomized controlled trial. JAMA 292(3):331-337.

Wittekoek ME, de Groot E, Prins MH, Trip MD, Buller HR, Kastelei JJ. 1999. Differences in intima-media thickness in the carotid and femoral arteries in familial hypercholesterolemic heterozygotes with and without clinical manifestations of cardiovascular disease. Atherosclerosis 146(2):271-279.

Zanobetti A, Schwartz J. 2002. Cardiovascular damage by airborne particles: are diabetics more susceptible? Epidemiology 13(5):588-592.

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Original Contribution

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Association of Low-Level Ozone and Fine Particles With Respiratory Symptoms in Children With Asthma

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ABSTRACT

Context Exposure to ozone and particulate matter of 2.5 μm or less ($PM_{2.5}$) in air at levels above current US Environmental Protection Agency (EPA) standards is a risk factor for respiratory symptoms in children with asthma.

Objective To examine simultaneous effects of ozone and $PM_{2.5}$ at levels below EPA standards on daily respiratory symptoms and rescue medication use among children with asthma.

Design, Setting, and Participants Daily respiratory symptoms and medication use were examined prospectively for 271 children younger than 12 years with physician-diagnosed, active asthma residing in southern New England. Exposure to ambient concentrations of ozone and $PM_{2.5}$ from April 1 through September 30, 2001, was assessed using ozone (peak 1-hour and 8-hour) and 24-hour $PM_{2.5}$. Logistic regression analyses using generalized estimating equations were performed separately for maintenance medication users (n = 130) and nonusers (n = 141). Associations between pollutants (adjusted for temperature, controlling for

same- and previous-day levels) and respiratory symptoms and use of rescue medication were evaluated.

Main Outcome Measures Respiratory symptoms and rescue medication use recorded on calendars by subjects' mothers.

Results Mean (SD) levels were 59 (19) ppb (1-hour average) and 51 (16) ppb (8-hour average) for ozone and 13 (8) $\mu g/m^3$ for $PM_{2.5}$. In copollutant models, ozone level but not $PM_{2.5}$ was significantly associated with respiratory symptoms and rescue medication use among children using maintenance medication; a 50-ppb increase in 1-hour ozone was associated with increased likelihood of wheeze (by 35%) and chest tightness (by 47%). The highest levels of ozone (1-hour or 8-hour averages) were associated with increased shortness of breath and rescue medication use. No significant, exposure-dependent associations were observed for any outcome by any pollutant among children who did not use maintenance medication.

Conclusion Asthmatic children using maintenance medication are particularly vulnerable to ozone, controlling for exposure to fine particles, at levels below EPA standards.

INTRODUCTION

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Children with asthma are particularly vulnerable to the adverse health effects of high levels of **air pollution**. Studies of children with asthma living in some of the most highly polluted regions of the world conclude that exposure to levels of ozone or particulate matter (especially particles ≤2.5 µm in diameter [$PM_{2.5}$]) regularly in excess of US Environmental Protection Agency (EPA) air quality standards (120 ppb [1-hour average] and 80 ppb [8-hour average] for ozone and 65 $\mu g/m^3$ for 24-hour $PM_{2.5}$) significantly enhances the risk of respiratory symptoms, asthma medication use, and reduced lung function.[1-5]

Studies of children with asthma living in regions with levels of pollution within or near compliance with EPA air quality standards suggest that the current standards do not protect these more vulnerable members of the population.[6-10] Asthma severity, as measured by symptoms, medication use, restrictions in activity, or use of medical services, has been shown to be affected by exposure to ozone (1-hour maximum measurement[6-10] or 8-hour average[6-9]), particles 10 µm or smaller (PM_{10}),[6, 8] or $PM_{2.5}$ (12-hour total).[6]

Of interest in many recent studies of children with asthma are the simultaneous effects of ozone and particulates on asthma severity.[2-3,8] Simultaneous exposure to high levels of both ozone and $PM_{2.5}$ (fine particles)[2] or PM_{10}(coarse particles)[3] found in Mexico City, Mexico, contributed to increased respiratory symptoms among children with asthma. In a region of lower pollution, asthma symptoms were associated with both ozone and course particles.[8] In the current study, we examined the simultaneous

effects of ozone and fine particles on daily respiratory symptoms and rescue medication use of children with asthma residing in southern New England during spring and summer 2001.

METHODS

Participants

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The study participants were 271 children from a cohort of families living in Connecticut and the Springfield area of Massachusetts who were participating in a study of asthma development.[11-12] From 1997 through 1999, 1002 infants born to families with at least 1 child with physician-diagnosed asthma were enrolled in the original birth cohort. Beginning in 2000, eligible asthmatic siblings (1 per cohort family) were identified and invited to participate in a 1-year prospective study of asthma severity. Eligibility criteria were that the child was younger than 12 years at the time of enrollment and had exhibited respiratory symptoms or used asthma medication within the previous 12 months. Included in the current analysis are subjects enrolled for all or part of the 183-day sampling period (April 1 through September 30, 2001), which includes the summertime, high-ozone pollution months in this region. Of 357 children identified as being eligible for inclusion in the current analysis, 56 refused follow-up, 16 were lost to follow-up, and 14 withdrew before April 1, 2001, leaving a total of 271 (76%). The Human Investigation Committee of Yale University, New Haven, Conn, approved this study, and all respondents (mothers of study subjects) gave informed consent before participation.

Data Collection

Demographic information and medical histories were collected during a home interview with the mother at enrollment. Daily respiratory symptoms (wheeze, persistent cough, chest tightness, shortness of breath) and medication use (maintenance medications, including inhaled or systemic steroids, cromolyn sodium, and leukotriene inhibitors, and rescue medications, including bronchodilators) were recorded on symptom and medication calendars by the child's mother and collected through monthly telephone interviews. Additional information about the previous 12 months was collected at an exit interview (eg, dates the child had been away from the southern New England region during the study year).

Air Quality Assessment

Study subjects resided in a 6691-square mile area in Connecticut and the Springfield area of Massachusetts. All ambient air quality monitoring sites (14 sites for ozone, 10 in Connecticut and 4 in Massachusetts; 4 sites for daily $PM_{2.5}$, 2 in Connecticut and 2 in Massachusetts; 13 temperature sites, 12 in Connecticut and 1 in Massachusetts) were located within a 52.5-mile radius centered at Southington, Conn (14 miles southwest of Hartford). The maximum distance between sites was 105 miles; the minimum distance was 4 miles. The Departments of Environmental Protection (DEPs) of Connecticut and Massachusetts provided measurements for hourly ozone concentrations and temperatures and daily 24-hour $PM_{2.5}$ (total $PM_{2.5}$ accumulated during 24

hours). Since both ozone and fine particle pollutants, as well as meteorological variables, tend to be regional,[13] the maximum daily 1-hour average (mean over 1 hour) and the 8-hour rolling average (mean over previous 8 hours) for ozone, daily $PM_{2.5}$ concentration, and maximum daily temperature were averaged across monitoring sites. Between-site correlation coefficients (Pearson *r*) were high for the 4 daily $PM_{2.5}$ sites (median $r = 0.91$; range, 0.84-0.95) and the 13 temperature sites (median $r = 0.97$; range, 0.85-0.99). There was more variability among the 14 ozone monitoring sites (median $r = 0.83$; range, 0.50-0.97 for the 1-hour average; and median $r = 0.81$; range, 0.47-0.97 for the 8-hour average). For technical details on ambient air quality monitoring, see the Web sites for the Connecticut DEP[14] and the Massachusetts DEP.[15]

Data Analysis

To examine the effects of ozone and $PM_{2.5}$ on children with different degrees of asthma severity, children were divided into 2 groups: those who used any maintenance medication during the 183-day observation period (n = 130) and those who did not (n = 141). Use of maintenance medication was used as a proxy for asthma severity to avoid using the outcome measures (respiratory symptoms and rescue medication use) in the assessment of severity. Logistic regression analyses, using generalized estimating equations (PROC GENMOD with AR1 autoregressive structure in SAS statistical software)[16-18] and adjusted for maximum daily temperature, were used to evaluate the association between levels of ozone and $PM_{2.5}$, with presence or absence of specific respiratory symptoms or rescue medication use. Using a repeated-measures technique permitted each subject to serve as his or her own control; therefore, personal variables (eg, race and other sociodemographic factors) that would not change during the study were not included in the models. Subgroup analysis, which included either 17 160 observations (an average of 132 days of data for 130 users of maintenance medication) or 19 035 observations (135 days for 141 nonusers of maintenance medication), focused directly on the association between exposures and health effects.

Exposure variables were categorized into quintiles, then entered into the model as dummy variables. The reference category for each was the lowest quintile. Both same-day and previous-day levels of ozone and $PM_{2.5}$ were examined. Analyses were performed separately for each severity group and each outcome. In single-pollutant models, a test for linear trend was performed by examining the model when the pollutant was entered as a continuous variable instead of as quintiles. In copollutant models, a test for goodness of fit was performed using the Hosmer-Lemeshow statistic for logistic regression. Significance level for all tests was set at .05.

RESULTS

Descriptive Statistics

Levels of ozone, $PM_{2.5}$, and temperature from April through September 2001 are summarized in Table 1 and Figure 1. The EPA 1-hour standard (120 ppb) was exceeded on 3 days, and the 8-hour ozone standard

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(80 ppb) was exceeded on 10 days of the 183 days of observation. There were no days when the level of $PM_{2.5}$ exceeded the EPA 24-hour standard of 65 $\mu g/m^3$. There was a strong correlation between ozone and fine particles ($PM_{2.5}$ vs 1-hour average ozone $r = 0.77$ vs 8-hour average $r = 0.74$) (Table 2).

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Table 1. Ozone, Particulate Matter of 2.5 µm or Less ($PM_{2.5}$), and Temperature in Southern New England, April 1 to September 30, 2001

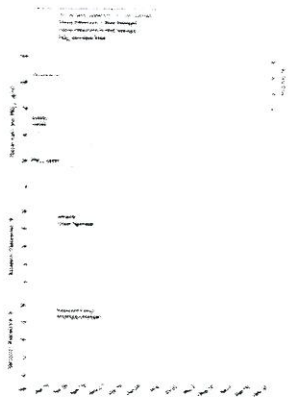

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Figure. Daily Levels of Ozone (Both 1-Hour Average and 8-Hour Average), Particulate Matter of 2.5 µm or Less ($PM_{2.5}$), and Daily Maximum Temperature, With Daily Prevalence of Respiratory Symptoms for Users of Asthma Maintenance Medication (n = 130) for Southern New England, April 1 through September 30, 2001

Dotted lines at 80 ppb and 120 ppb indicate Environmental Protection Agency standards for 8-hour average and 1-hour average ozone, respectively. Note that daily exposure levels shown here are the result of averaging over regional monitoring sites (14 ozone, 4 $PM_{2.5}$, and 13 temperature sites).

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Table 2. Pearson Correlation Coefficients for Same Day and Previous Day Levels of Ozone and Particulate Matter of 2.5 µm or Less ($PM_{2.5}$)

There were no significant differences between the users (n = 130) of maintenance medication and nonusers (n = 141) for mean (SD) age of study subjects (age on April 1, 2001, for users, 8.8 [2.0] years [range, 2.4-12.7 years]; age of nonusers, 8.3 [2.2] years [range, 2.0-12.6 years]; *t* test $P = .71$) or mean days of participation (mean participation for users, 132 [48] days [range, 3-183 days]; mean participation for nonusers, 135 [51] days [range, 5-183 days]; *t* test $P = .50$). Sex and ethnicity did not differ by medication use. Nearly two thirds of each group were male (users, 64.6%; nonusers, 64.5%; χ^2 test $P = .99$), and most

children in each group were white, with smaller numbers of black and Hispanic children (users, 80.0%, 8.5%, and 11.5%, respectively; nonusers, 70.9%, 11.4%, and 17.7%, respectively; χ^2 test $P = .22$). Compared with nonusers of maintenance medication, users had significantly more days of all respiratory symptoms and rescue medication use: 50% of this group experienced approximately 1 week of persistent cough or wheeze, had 2 to 3 days of chest tightness or shortness of breath, and used rescue medication for nearly 3 weeks during the 26-week study period. At least half of all nonusers experienced no symptoms and did not use rescue medication during this same period (Table 3). Daily prevalence of symptoms for users of maintenance medication is shown in Figure 1. With the exception of somewhat higher rates of symptoms in the early spring and late summer when the temperatures tended to be lowest, there was overall conformity of reporting all 4 symptoms across the observation period.

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Table 3. Rates of Respiratory Symptoms and Rescue Medication Use for Study Subjects Stratified by Use of Maintenance Medication (Southern New England, April 1-September 30, 2001)*

Single-Pollutant Models for Users of Maintenance Medication

Ozone (1-Hour Average). An ozone concentration of 51.6 ppb or higher (the top 3 quintiles of the distribution of the maximum 1-hour average) on the same day as the reported symptom was the only exposure variable associated with an increased likelihood of wheeze (by 16%, 16%, and 22%, respectively) (Table 4, model 1). A 4% increase in bronchodilator use was also associated with same-day levels of ozone (51.6-58.8 ppb) (Table 4, model 1). Previous-day levels of maximum 1-hour average ozone were associated with increased likelihoods of persistent cough (16% increase for levels ≥72.7 ppb), chest tightness (by 21%, 30%, and 37% for levels ≥51.6 ppb), and shortness of breath (by 22% and 30% for levels ≥58.9 ppb) (Table 4, Model 2). The effects of previous-day levels on chest tightness and shortness of breath were significant in an exposure-dependent way: for each 50-ppb increase in previous-day, 1-hour ozone levels, the likelihood of these symptoms increased by 26% (odds ratio [OR], 1.26; 95% confidence interval [CI], 1.0-1.48) and 22% (OR, 1.22; 95% CI, 1.02-1.45), respectively.

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Table 4. Odds Ratios From 6 Single-Pollutant Logistic Regression Models of Respiratory Symptoms or Rescue Medication Use of Maintenance Medication Users (n = 130) (Southern New England, April 1 to September 30, 2001)*

Ozone (8-Hour Average). An ozone concentration of 63.3 ppb or higher, measured as the maximum 8-hour average on the same day as the reported symptom, was associated with a 30% increase in chest tightness (Table 4, model 3). Previous-day levels of 52.1 ppb or higher were associated with increased chest tightness, persistent cough, and shortness of breath (Table 4, model 4). As was the case with 1-hour ozone levels, the associations with the symptoms of chest tightness and shortness of

breath were exposure dependent: a 50-ppb increase in previous-day, 8-hour ozone level increased the likelihood of chest tightness (OR, 1.33; 95% CI, 1.09-1.62) and shortness of breath (OR, 1.30; 95% CI, 1.05-1.61).

$PM_{2.5}$. Increased likelihood of chest tightness was associated with same-day levels of $PM_{2.5}$ from 12.1 to 18.9 $\mu g/m^3$ (Table 4, model 5). Previous-day levels of 19.0 $\mu g/m^3$ or higher were associated with persistent cough, chest tightness, and shortness of breath (Table 4, model 6).

Copollutant Models for Users of Maintenance Medication

In logistic regression models of both ozone and fine particles for children taking maintenance medication, an increased likelihood of respiratory symptoms was associated with levels of ozone on the same day, previous day, or both; and increased bronchodilator use was associated with the highest level of same-day ozone. Neither respiratory symptoms nor bronchodilator use were associated with level of fine particles.

Ozone (1-Hour Average) and $PM_{2.5}$. Increased likelihood of wheeze was associated with same-day levels of 1-hour average ozone of 43.2 ppb or higher in an exposure-dependent manner (Table 5). When ozone is entered into this same model as a continuous variable, a 50-ppb increase in same-day ozone increases the likelihood of wheeze by 35% (OR, 1.35; 95% CI, 1.11-1.65). None of the exposure variables was associated with an increased likelihood of persistent cough, and only 1-hour average ozone levels between 43.2 and 51.5 ppb were associated with a decreased likelihood of cough (OR, 0.88; 95% CI, 0.78-0.99). The likelihood of chest tightness was significantly increased by same-day (≥58.9 ppb) and previous-day (≥51.6 ppb) levels of ozone in an exposure-dependent way. The likelihood of chest tightness increases by 47% (OR, 1.47; 95% CI, 1.18-1.84) for each 50-ppb increase in same-day levels of ozone, and by 42% (OR, 1.42; 95% CI, 1.14-1.78) for each 50-ppb increase in previous-day levels. Shortness of breath and ozone were similarly associated; likelihood of the symptom was increased by same-day levels of 72.7 ppb or higher and previous-day levels from 58.9 to 72.6 ppb (by 32%). Increased likelihood of bronchodilator use was associated with same-day levels of 72.7 ppb or higher (Table 5).

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Table 5. Odds Ratios From the Copollutant Logistic Regression Model for Same-Day and Previous-Day Levels of Ozone (1-Hour Average) and Particulate Matter of 2.5 µm or Less ($PM_{2.5}$) Related to Each Respiratory Symptom or Rescue Medication Use of Maintenance Medication Users (n = 130) (Southern New England, April 1 to September 30, 2001)*

Ozone (8-Hour Average) and $PM^{2.5}$. For 8-hour average ozone levels, the likelihood of chest tightness was increased by same-day (OR, 1.64; 95% CI, 1.23-2.17) and previous-day (OR, 1.45; 95% CI, 1.10-1.92) levels of 63.3 ppb or higher. Shortness of breath was similarly associated; likelihood of the symptom was increased by same-day (OR, 1.45; 95% CI, 1.10-1.91) and

previous-day (OR, 1.31; 95% CI, 1.00-1.71) levels of 63.3 ppb or higher. As seen for the highest 1-hour ozone level, increased bronchodilator use was associated with same-day levels of 63.3 ppb or higher for 8-hour ozone measurements (OR, 1.09; 95% CI, 1.02-1.17).

Nonusers of Maintenance Medication

Single-Pollutant Models. Similar analyses for nonusers of maintenance medication revealed no significant associations among the top 3 concentration quintiles for the exposure variables and respiratory symptoms or bronchodilator use. For example, chest tightness was not significantly associated with same-day, 1-hour ozone levels of 72.7 ppb or higher (OR, 0.92; 95% CI, 0.68-1.25), same-day, 8-hour ozone levels of 63.3 ppb or higher (OR, 1.17; 95% CI, 0.72-1.92), or previous-day, 8-hour ozone levels of 63.3 ppb or higher (OR, 0.99; 95% CI, 0.74-1.35). The only significant association was an increased likelihood of wheeze (OR, 1.20; 95% CI, 1.00-1.43) in the presence of previous-day, 8-hour average ozone between 39.1 and 45.8 ppb (the second quintile).

Copollutant Models. For the children who were not users of asthma maintenance medication, neither fine particles nor 1-hour average ozone levels were associated with increased likelihoods of respiratory symptoms in copollutant models. Increased bronchodilator use was associated with previous-day fine particle concentrations between 9.0 and 12.0 $\mu g/m^3$ in the model with 1-hour ozone levels (Table 6) and with these same levels in the model with 8-hour ozone (OR, 1.30; 95% CI, 1.02-1.65). An increase in the likelihood of wheeze was associated with 8-hour ozone, but only for concentrations between 39.1 and 45.8 ppb on the same day (OR, 1.33; 95% CI, 1.00-1.77) or the previous day (OR, 1.31; 95% CI, 1.05-1.63) and between 52.1 and 63.2 ppb for same-day levels (OR, 1.35; 95% CI, 1.00-1.81).

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Table 6. Odds Ratios From the Copollutant Logistic Regression Model for Same-Day and Previous-Day Levels of Ozone (1-Hour Average) and Particulate Matter of 2.5 µm or Less ($PM_{2.5}$) Related to Respiratory Symptoms and Rescue Medication Use of Maintenance Medication Nonusers (n = 141) (Southern New England, April 1 to September 30, 2001)*

COMMENT

In models controlling for ambient fine particle concentration and typically at levels below EPA air quality standards, daily ambient ozone was found to be significantly associated with increased risk of respiratory symptoms and increased use of rescue medication among children with asthma severe enough to require maintenance medication. Study strengths include frequent telephone follow-up to collect information on daily calendar-recorded symptoms and medication use; absence of reporting bias between symptoms and

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regionally collected ambient air quality data; the use of both the maximum 1-hour average (sensitive to spikes in concentration) and 8-hour average (a measure of short-term, cumulative exposure) to assess daily ambient ozone levels; use of $PM_{2.5}$ levels measured daily; and examination of the simultaneous effects of ozone and $PM_{2.5}$ at levels near or below current EPA ambient standards. Our results contribute to the limited literature examining the simultaneous effects of ozone and suspended particles on daily respiratory symptoms for a sensitive subpopulation in models adjusted for daily temperature.

One potential limitation of the study is that ambient ozone and particle concentrations were represented as means over regional sites. For the 14 ozone sites on any particular day, the mean (SD) ratio of maximum to minimum reading was 1.70 (0.50), which is similar to the mean ratio of upper to lower limit of each quintile of the summer ozone distribution of 1.38 (0.30) from our study. This suggests that the analysis using quintiles of the ozone distribution captures the variability that exists in the study region. Variability among $PM_{2.5}$ sites was less, but a potential limitation is that there were only 4 sites with daily measurements. However, a comparison between readings from these 4 sites and readings from the 10 sites with $PM_{2.5}$ readings every 3 days revealed good agreement. For the 61 days all sites had in common, the 10-site mean (SD) was 13.8 (8.2) compared with 12.8 (7.7) $\mu g/m^3$ for the 4 sites, and the Pearson correlation was 0.97.

Another potential limitation is the lack of personal variables (eg, race) in the regression models. However, by taking advantage of the repeated measurements we had for each subject, we were able to use each subject as his or her own control. The sample of 271 children contributed 36 195 person-days of observations to the analyses. Our within-subjects analytic approach permitted a strong test of the associations between ambient **air pollution** and health outcomes, and personal variables, since they would not vary within subjects, could be excluded from the models.

In this study, we did not consider medical care utilization as an outcome. Since this was not a clinic-based study, we did not have access to records to confirm medical visit dates. However, medical records are not necessarily more objective than reports of symptoms and medication use, since a number of factors unrelated to symptom severity also influence utilization. Symptoms and medication use vary from day to day and may be a more sensitive indicator of the effects of daily changes in **air pollution** on respiratory health, since not all symptoms result in a physician visit.

In our copollutant models, ozone but not fine particles significantly predicted increased risk of respiratory symptoms and rescue medication use among children using asthma maintenance medication. We found an immediate (same-day) effect of ozone on wheeze (with the 1-hour ozone metric), chest tightness, and shortness of breath (with both the 1-hour and 8-hour ozone metrics). We also found that previous-day levels of ozone (both metrics) were significantly associated with increased risk of chest tightness and shortness of breath. Goodness-of-fit tests for copollutant models suggest that the models with significant findings (wheeze, chest tightness, and shortness of breath) are reasonably good fits to the data. There were no systematic patterns to the lack of fit for models for persistent cough and bronchodilator use. However, because of repeated measurements, observations were not independent in any of the models, which may affect the interpretation of the Hosmer-Lemeshow statistic. It is possible that the

more frequently reported events of persistent cough and bronchodilator use may be associated with ambient **air pollution** in combination with other factors (eg, activity level) not included in the current study.

Effects of 1-hour ozone among children using asthma maintenance medication, especially the association of same-day ozone with wheeze and previous-day ozone with chest tightness, appear to be more exposure dependent than the effects of small particles. In copollutant models for wheeze and chest tightness, a 50-ppb increase in same-day, 1-hour ozone level increased the likelihood of wheeze by 35% and chest tightness by 47%. However, since particles and ozone were positively correlated, it is difficult to separate their effects in the copollutant models. In the single-pollutant model for chest tightness, a 50-ppb increase in previous-day levels of 1-hour ozone resulted in a 26% increase in the likelihood of having the symptom. When same-day levels of 1-hour ozone were added to the model, the likelihood of this symptom went up to 32%. In the copollutant model, a 50-ppb increase in previous-day, 1-hour ozone level increased the likelihood of chest tightness by 42%. Levels of $PM_{2.5}$ happened to be relatively low and never exceeded EPA standards for the duration of the study period, which likely contributed to the lack of significant particle effects observed in the copollutant models. For our region, an examination of the association between symptoms and particle levels in winter months when ozone is not a factor would help us better understand the role of exposure to small particles on respiratory health.

There is little doubt that children with asthma are especially vulnerable to high levels of **air pollution**. Among a group of asthmatic children (n = 71) living in Mexico City, where levels of ozone have regularly exceeded the EPA standard, multivariate regression analyses of same-day ambient **air pollution** and separate models of previous-day pollution all revealed significant effects of ozone and fine particles on the likelihood of cough (an increase of 8% for each 50-ppb increase in ozone on either the same day or previous day; an increase of 6% or 8% for each 10-$\mu g/m^3$ increase in $PM_{2.5}$ on the same day or previous day) and lower respiratory tract illness (by 7% for each pollutant on the same day or previous day).[2] The effects seen for $PM_{2.5}$ in Mexico City, but not in our study, could be explained by the large difference between the mean (SD) 24-hour concentration of $PM_{2.5}$ in Mexico City (85.7 [30.2] $\mu g/m^3$), which was above the EPA standard of 65 $\mu g/m^3$ and was well above the mean of 13.1 (7.9) $\mu g/m^3$ observed in the current study. In addition, the chemical composition of the fine particles in each region may be different.[2, 10] The larger effect of 1-hour ozone that we found could be explained in part by the fact that we stratified our analysis by asthma severity, thereby observing a consistent pattern of increased likelihood of some symptoms of more than 40% in the group with more severe disease and no significant effects among the group with less severe disease.

Our results are consistent with recent studies[7, 10] that suggest exposure to lower levels of ozone is associated with respiratory symptoms in children with asthma. Children with asthma who attended a week-long asthma summer camp (a total of 166 children during three 1-week periods compared with our 183-day observation period) in the Connecticut River Valley (the same geographic area as the current study) were exposed to levels of ozone somewhat higher than the current study (mean [SD] 1-hour average, 84 [38] ppb; range, 20-160 ppb). In single-pollutant models, daily levels of same-day ozone were significantly associated with increased chest symptoms, β-agonist use, and decreased lung function.[10] These associations did not change when same-day

levels of sulfate (a primary constituent of $PM_{2.5}$ in this region) were added to the model. In a recent study[7] of 846 children with asthma living in 8 urban areas around the country, ozone at levels comparable to those observed in the current study (mean 8-hour average of 48 ppb compared with our mean of 51 ppb with <5% of the days exceeding the EPA standard of 80 ppb in both studies) was associated, in single-pollutant models, with morning respiratory symptoms (wheeze, cough, or chest tightness). Although the data were not shown, the authors of each study also noted that adding copollutants to their models did not appreciably confound the effect of ozone. Both studies concluded that ozone, even at levels lower than current EPA standards, is strongly associated with adverse respiratory health effects in children with asthma.

Previous environmental chamber studies[19-21] of adults with asthma exposed to ozone for 1 to a few hours have shown relatively little effect on symptoms or lung function. On the other hand, short-term exposure to elevated levels of ozone and particulates in outdoor air has been associated with reduced pulmonary function in otherwise healthy children.[1, 22-23] Our study of asthmatic children under ambient exposure conditions in areas of lower pollution suggests that the more prolonged exposures associated with summertime ozone produce a greater stimulus than chamber exposures, that asthmatic children are more susceptible than asthmatic adults, that effects are delayed and not captured by short-term chamber studies, or that coexposures to other unidentified constituents of ambient air enhance the response to ozone. A recent study supporting this view examined the impact of traffic-reducing changes in Atlanta, Ga, during the 1996 summer Olympic Games.[24] Significant reductions in ozone and particles were associated with significant reductions in acute asthma care events (physician, clinic, or hospital visits) among children aged 1 to 16 years. In analyses including days before, during, and after the Olympics, an increase in daily acute asthma events was associated with levels of 1-hour ozone concentrations beginning at 60 to 89 ppb. Our findings indicate that comparable levels were associated with an increased likelihood of wheeze (≥58.9 ppb), chest tightness (≥58.9 ppb), shortness of breath, and rescue medication use (≥72.7 ppb).

In our study, we defined 2 levels of asthma severity based on maintenance medication use. We reasoned that since we were examining the association of **air pollution** and symptoms, we did not want to use symptoms to define severity. Instead, we used maintenance medication as a proxy for disease severity even though medication use and symptoms will be related. Maintenance medication users had significantly more wheeze, persistent cough, chest tightness, and shortness of breath than the nonusers and used rescue medication significantly more often. Our results strongly suggest that this definition of asthma severity divides the group into 2 levels of vulnerability to **air pollution**.

Our study is a unique combination of a sample of asthmatic children with detailed symptom and medication use followed for a long period and well-measured daily ambient copollutants. These results add to others that suggest that, even at low levels of ambient ozone and controlling for ambient fine particle concentration, children with severe asthma are at a significantly increased risk of experiencing respiratory symptoms.

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1. Gold DR, Damokosh AI, Pope CA III, et al. Particulate and ozone pollutant effects on the respiratory function of children in southwest Mexico City. *Epidemiology.* 1999;10:8-16. ISI | MEDLINE

2. Romieu I, Meneses F, Ruiz S, et al. Effects of **air pollution** on the respiratory health of asthmatic children living in Mexico City. *Am J Respir Crit Care Med.* 1996;154:300-307. ABSTRACT

3. Romieu I, Meneses F, Ruiz S, et al. Effects of intermittent ozone exposure on peak expiratory flow and respiratory symptoms among asthmatic children in Mexico City. *Arch Environ Health.* 1997;52:368-376. ISI | MEDLINE

4. Peters A, Dockery DW, Heinrich J, Wichmann HE. Medication use modifies the health effects of particulate sulfate **air pollution** in children with asthma. *Environ Health Perspect.* 1997;105:430-435. ISI | MEDLINE

5. Ostro BD, Lipsett MJ, Mann JK, Braxton-Owens H, White MC. **Air pollution** and asthma exacerbations among African-American children in Los Angeles. *Inhal Toxicol.* 1995;7:711-722. ISI

6. Ostro B, Lipsett M, Mann J, Braxton-Owens H, White M. **Air pollution** and exacerbation of asthma in African-American children in Los Angeles. *Epidemiology.* 2001;12:200-208. CrossRef | ISI | MEDLINE

7. Mortimer KM, Tager IB, Dockery DW, Neas LM, Redline S. The effect of ozone on inner-city children with asthma: identification of susceptible subgroups. *Am J Respir Crit Care Med.* 2000;162:1838-1845. ABSTRACT/FULL TEXT

8. Delfino RJ, Zeiger RS, Seltzer JM, Street DH. Symptoms in pediatric asthmatics and **air pollution**: differences in effects by symptom severity, anti-inflammatory medication use and particulate averaging time. *Environ Health Perspect.* 1998;106:751-761. ISI | MEDLINE

9. Gielen MH, van der Zee SC, van Wijnen JH, van Steen CJ. Acute effects of summer **air pollution** on respiratory health of asthmatic children. *Am J Respir Crit Care Med.* 1997;155:2105-2108. ABSTRACT

10. Thurston GD, Lippmann M, Scott MB, Fine JM. Summertime haze **air pollution** and children with asthma. *Am J Respir Crit Care Med.* 1997;155:654-660. ABSTRACT

11. Gent JF, Ren P, Belanger K, et al. Levels of household mold associated with respiratory symptoms in the first year of life in a cohort at risk for asthma. *Environ Health Perspect.* 2002;110:A781-A786. ISI | MEDLINE

12. Belanger K, Beckett W, Triche E, et al. Symptoms of wheeze and persistent cough in the first year of life: associations with indoor allergens, air contaminants, and maternal history of asthma. *Am J Epidemiol.* 2003;158:195-202. ABSTRACT/FULL TEXT

13. US Environmental Protection Agency. *Air Quality Criteria for Ozone and Related Photochemical Oxidants.* Research Triangle Park, NC: Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office; 1996. EPA report EPA/600/AP-93/004a-c.

14. State of Connecticut Department of Environmental Protection. Annual Air Quality Summary (1999). Available at: http://dep.state.ct.us/air2/ozone/99aqs.pdf. Accessed November 18, 2002.

15. Commonwealth of Massachusetts Department of Environmental Protection. Air Quality Report (2000). Available at: http://www.mass.gov/dep/bwp/daqc. Accessed November 18, 2002.

16. SAS Version 8. Cary, NC: SAS Institute Inc; 2001.

17. Liang K-Y, Zeger SL. Longitudinal data analysis using generalized linear models. *Biometrika.* 1986;73:13-22. ISI

18. Allison PD. *Logistic Regression Using the SAS System: Theory and Application*. Cary, NC: SAS Institute Inc; 1999.

19. Silverman F. Asthma and respiratory irritants (ozone). *Environ Health Perspect.* 1979;29:131-136. ISI | MEDLINE

20. Hanania NA, Tarlo SM, Silverman F, Urch B, Senathirajah N, Zamel N, Corey P. Effect of exposure to low levels of ozone on the response to inhaled allergen in allergic asthmatic patients. *Chest.* 1998;114:752-756. ABSTRACT/FULL TEXT

21. Kehrl HR, Peden DB, Ball B, Folinsbee LJ, Horstman D. Increased specific airway reactivity of persons with mild allergic asthma after 7.6 hours of exposure to 0.16 ppm ozone. *J Allergy Clin Immunol.* 1999;104:1198-1199. ISI | MEDLINE

22. Spektor DM, Lippmann M, Lioy PJ, et al. Effects of ambient ozone on respiratory function in active normal children. *Am Rev Respir Dis.* 1988;137:313-320. ISI | MEDLINE

23. Ulmer C, Kopp M, Ihorst G, Frischer T, Forster J, Kuehr J. Effects of ambient ozone exposures during the spring and summer of 1994 on pulmonary function of schoolchildren. *Pediatr Pulmonol.* 1997;23:344-353. CrossRef | ISI | MEDLINE

24. Friedman MS, Powell KE, Hutwagner L, Graham LM, Teague WG. Impact of changes in transportation and commuting behaviors during the 1996 summer Olympic Games in Atlanta on air quality and childhood asthma. *JAMA.* 2001;285:897-905. ABSTRACT/FULL TEXT

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Original Contribution

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Lung Cancer, Cardiopulmonary Mortality, and Long-term Exposure to Fine Particulate Air Pollution

C. Arden Pope III, PhD; Richard T. Burnett, PhD; Michael J. Thun, MD; Eugenia E. Calle, PhD; Daniel Krewski, PhD; Kazuhiko Ito, PhD; George D. Thurston, ScD

JAMA. 2002;287:1132-1141.

ABSTRACT

Context Associations have been found between day-to-day particulate air pollution and increased risk of various adverse health outcomes, including cardiopulmonary mortality. However, studies of health effects of long-term particulate air pollution have been less conclusive.

Objective To assess the relationship between long-term exposure to fine particulate air pollution and all-cause, lung cancer, and cardiopulmonary mortality.

Design, Setting, and Participants Vital status and cause of death data were collected by the American Cancer Society as part of the Cancer Prevention II study, an ongoing prospective mortality study, which enrolled approximately 1.2 million adults in 1982. Participants completed a questionnaire detailing individual risk factor data (age, sex, race, weight, height, smoking history, education, marital status, diet, alcohol consumption, and occupational exposures). The risk factor data for approximately 500 000 adults were linked with air pollution data for metropolitan areas throughout the United States and combined with vital status and cause of death data through December 31, 1998.

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Main Outcome Measure All-cause, lung cancer, and cardiopulmonary mortality.

Results Fine particulate and sulfur oxide–related pollution were associated with all-cause, lung cancer, and cardiopulmonary mortality. Each 10-μg/m^3 elevation in fine particulate air pollution was associated with approximately a 4%, 6%, and 8% increased risk of all-cause, cardiopulmonary, and lung cancer mortality, respectively. Measures of coarse particle fraction and total suspended particles were not consistently associated with mortality.

Conclusion Long-term exposure to combustion-related fine particulate air pollution is an important environmental risk factor for cardiopulmonary and lung cancer mortality.

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Based on several severe air pollution events,[1-3] a temporal correlation between extremely high concentrations of particulate and sulfur oxide air pollution and acute increases in mortality was well established by the 1970s. Subsequently, epidemiological studies published between 1989 and 1996 reported health effects at unexpectedly low concentrations of particulate air pollution.[4] The convergence of data from these studies, while controversial,[5] prompted serious reconsideration of standards and health guidelines[6-10] and led to a long-term research program designed to analyze health-related effects due to particulate pollution.[11-13] In 1997, the Environmental Protection Agency adopted new ambient air quality standards that would impose regulatory limits on fine particles measuring less than 2.5 μm in diameter ($PM_{2.5}$). These new standards were challenged by industry groups, blocked by a federal appeals court, but ultimately upheld by the US Supreme Court.[14]

Although most of the recent epidemiological research has focused on effects of short-term exposures, several studies suggest that long-term exposure may be more important in terms of overall public health.[4] The new standards for long-term exposure to $PM_{2.5}$ were originally based primarily on 2 prospective cohort studies,[15-16] which evaluated the effects of long-term pollution exposure on mortality. Both of these studies have been subjected to much scrutiny,[5] including an extensive independent audit and reanalysis of the original data.[17] The larger of these 2 studies linked individual risk factor and vital status data with national ambient air pollution data.[16] Our analysis uses data from the larger study and (1) doubles the follow-up time to more than 16 years and triples the number of deaths; (2) substantially expands exposure data, including gaseous copollutant data and new $PM_{2.5}$ data, which have been collected since the promulgation of the new air quality standards; (3) improves control of occupational exposures; (4) incorporates dietary variables that account for total fat consumption, and consumption of vegetables, citrus, and high-fiber grains; and (5) uses recent advances in statistical modeling, including the incorporation of random effects and nonparametric spatial smoothing components in the Cox proportional hazards model.

METHODS

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Study Population

The analysis is based on data collected by the American Cancer Society (ACS) as part of the Cancer Prevention Study II (CPS-II), an ongoing prospective mortality study of approximately 1.2 million adults.[18-19] Individual participants were enrolled by ACS volunteers in the fall of 1982. Participants resided in all 50 states, the District of Columbia, and Puerto Rico, and were generally friends, neighbors, or acquaintances of ACS volunteers. Enrollment was restricted to persons who were aged 30 years or older and who were members of households with at least 1 individual aged 45 years or older. Participants completed a confidential questionnaire, which included questions about age, sex, weight, height, smoking history, alcohol use, occupational exposures, diet, education, marital status, and other characteristics.

Vital status of study participants was ascertained by ACS volunteers in September of the following years: 1984, 1986, and 1988. Reported deaths were verified with death certificates. Subsequently, through December 31, 1998, vital status was ascertained through automated linkage of the CPS-II study population with the National Death Index.[19] Ascertainment of deaths was more than 98% complete for the period of 1982-1988 and 93% complete after 1988.[19] Death certificates or codes for cause of death were obtained for more than 98% of all known deaths. Cause of death was coded according to the *International Classification of Diseases, Ninth Revision (ICD-9)*. Although the CPS-II cohort included approximately 1.2 million participants with adequate questionnaire and cause-of-death data, our analysis was restricted to those participants who resided in US metropolitan areas with available pollution data. The actual size of the analytic cohort varied depending on the number of metropolitan areas for which pollution data were available. Table 1 provides the number of metropolitan areas and participants available for each source of pollution data.

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Table 1. Summary of Alternative Pollution Indices*

Air Pollution Exposure Estimates

Each participant was assigned a metropolitan area of residence based on address at time of enrollment and 3-digit ZIP code area.[20] Mean (SD) concentrations of air pollution for the metropolitan areas were compiled from various primary data sources (Table 1). Many of the particulate pollution indices, including $PM_{2.5}$, were available from data from the Inhalable Particle Monitoring Network for 1979-1983 and data from the National Aerometric Database for 1980-1981, periods just prior to or at the beginning of the follow-up period. An additional data source was the Environmental Protection Agency Aerometric Information

Retrieval System (AIRS). The mean concentration of each pollutant from all available monitoring sites was calculated for each metropolitan area during the 1 to 2 years prior to enrollment.[17]

Additional information on ambient pollution during the follow-up period was extracted from the AIRS database as quarterly mean values for each routinely monitored pollutant for 1982 through 1998. All quarterly averages met summary criteria imposed by the Environmental Protection Agency and were based on observations made on at least 50% of the scheduled sampling days at each site. The quarterly mean values for all stations in each metropolitan area were calculated across the study years using daily average values for each pollutant except ozone. For ozone, daily 1-hour maximums were used and were calculated for the full year and for the third quarter only (ie, July, August, September). While gaseous pollutants generally had recorded data throughout the entire follow-up period of interest, the particulate matter monitoring protocol changed in the late 1980s from total suspended particles to particles measuring less than 10 μm in diameter (PM_{10}), resulting in the majority of total suspended particle data being available in the early to mid-1980s and PM_{10} data being mostly available in the early to mid-1990s.

As a consequence of the new $PM_{2.5}$ standard, a large number of sites began collecting $PM_{2.5}$ data in 1999. Daily $PM_{2.5}$ data were extracted from the AIRS database for 1999 and the first 3 quarters of 2000. For each site, quarterly averages for each of the 2 years were computed. The 4 quarters were averaged when at least 1 of the 2 corresponding quarters for each year had at least 50% of the sixth-day samples and at least 45 total sampling days available. Measurements were averaged first by site and then by metropolitan area. Although no network of $PM_{2.5}$ monitoring existed in the United States between the early 1980s and the late 1990s, the integrated average of $PM_{2.5}$ concentrations during the period was estimated by averaging the $PM_{2.5}$ concentration for early and later periods.

Mean sulfate concentrations for 1980-1981 were available for many cities based on data from the Inhalable Particle Monitoring Network and the National Aerometric Database. Recognizing that sulfate was artifactually overestimated due to glass fiber filters used at that time, season and region-specific adjustments were made.[17] Since few states analyzed particulate samples for sulfates after the early 1980s, individual states were directly contacted for data regarding filter use. Ion chromatography was used to analyze PM_{10} filters and this data could be obtained from metropolitan areas across the United States. Filters were collected for a single reference year (1990) in the middle of the 1982-1998 study period. The use of quartz filters virtually eliminated the historical overestimation of sulfate. Mean sulfate concentrations for 1990 were estimated using sulfate from AIRS, data reported directly from individual states, and analysis of archived filters.

Statistical Analysis

The basic statistical approach used in this analysis is an extension of the standard Cox proportional hazards survival model,[21] which has been used for risk estimates of pollution-related mortality in previous longitudinal cohort studies.[15-16] The standard Cox model implicitly assumes that observations are statistically independent after controlling for available risk factors, resulting in 2

concerns with regard to risk estimates of pollution-related mortality.[22] First, if the assumption of statistical independence is not valid, the uncertainty in the risk estimates of pollution-related mortality may be misstated. Second, even after controlling for available risk factors, survival times of participants living in communities closer together may be more similar than participants living in communities farther apart, which results in spatial autocorrelation. If this spatial autocorrelation is due to missing or systematically mismeasured risk factors that are spatially correlated with air pollution, then the risk estimates of pollution-related mortality may be biased due to inadequate control of these factors. Therefore, in this analysis, the Cox proportional hazards model was extended by incorporating a spatial random-effects component, which provided accurate estimates of the uncertainty of effect estimates. The model also evaluated spatial autocorrelation and incorporated a nonparametric spatial smooth component (to account for unexplained spatial structure). A more detailed description of this modeling approach is provided elsewhere.[22]

The baseline analysis in this study estimated adjusted relative risk (RR) ratios for mortality by using a Cox proportional hazards model with inclusion of a metropolitan-based random-effects component. Model fitting involved a 2-stage process. In the first stage, survival data were modeled using the standard Cox proportional hazards model, including individual level covariates and indicator variables for each metropolitan area (without pollution variables). Output from stage 1 provided estimates of the metropolitan-specific logarithm of the RRs of mortality (relative to an arbitrary reference community), which were adjusted for individual risk factors. The correlation between these values, which was induced by using the same reference community, was then removed.[23] In the second stage, the estimates of adjusted metropolitan-specific health responses were related to fine particulate air pollution using a linear random-effects regression model.[24] The time variable used in the models was survival time from the date of enrollment. Survival times of participants who did not die were censored at the end of the study period. To control for age, sex, and race, all of the models were stratified by 1-year age categories, sex, and race (white vs other), which allowed each category to have its own baseline hazard. Models were estimated for all-cause mortality and for 3 separate mortality categories: cardiopulmonary (*ICD-9* 401-440 and 460-519), lung cancer (*ICD-9* 162), and all others.

Models were estimated separately for each of the 3 fine particle variables, $PM_{2.5}$ (1979-1983), $PM_{2.5}$ (1999-2000), and $PM_{2.5}$ (average). Individual level covariates were included in the models to adjust for various important individual risk factors. All of these variables were classified as either indicator (ie, yes/no, binary, dummy) variables or continuous variables. Variables used to control for tobacco smoke, for example, included both indicator and continuous variables. The smoking indicator variables included: current cigarette smoker, former cigarette smoker, and a pipe or cigar smoker only (all vs never smoking) along with indicator variables for starting smoking before or after age 18 years. The continuous smoking variables included: current smoker's years of smoking, current smoker's years of smoking squared, current smoker's cigarettes per day, current smoker's cigarettes per day squared, former smoker's years of smoking, former smoker's years of smoking squared, former smoker's cigarettes per day, former smoker's cigarettes per day squared, and the number of hours per day exposed to passive cigarette smoke.

To control for education, 2 indicator variables, which indicated completion of high school or education beyond high school, were included. Marital status variables included indicator variables for single and other vs married. Both body mass index (BMI) values and BMI values squared were included as continuous variables. Indicator variables for beer, liquor, and wine drinkers and

nonresponders vs nondrinkers were included to adjust for alcohol consumption. Occupational exposure was controlled for using various indicator variables: regular occupational exposure to asbestos, chemicals/acids/solvents, coal or stone dusts, coal tar/pitch/asphalt, diesel engine exhaust, or formaldehyde, and additional indicator variables that indicated 9 different rankings of an occupational dirtiness index that has been developed and described elsewhere.[17, 25] Two diet indices that accounted for fat consumption and consumption of vegetables, citrus, and high-fiber grains were derived based on information given in the enrollment questionnaire.[18] Quintile indicator variables for each of these diet indices were also included in the models.[18]

In addition to the baseline analysis, several additional sets of analysis were conducted. First, to more fully evaluate the shape of the concentration-response function, a robust locally weighted regression smoother[26] (within the generalized additive model framework[27]) was used to estimate the relationship between particulate air pollution and mortality in the second stage of model fitting. Second, the sensitivity of the fine particle mortality risk estimates compared with alternative modeling approaches and assumptions was evaluated. Standard Cox proportional hazards models were fit to the data including particulate air pollution as a predictor of mortality and sequentially adding (in a controlled forward stepwise process) groups of variables to control for smoking, education, marital status, BMI, alcohol consumption, occupational exposures, and diet.

In addition, to evaluate the sensitivity of the estimated pollution effect while more aggressively controlling for spatial differences in mortality, a 2-dimensional term to account for spatial trends was added to the models and was estimated using a locally weighted regression smoother. The "span" parameter, which controls the complexity of the surface smooth, was set at 3 different settings to allow for increasingly aggressive fitting of the spatial structure. These included a default span of 50%, the span that resulted in the lowest unexplained variance in mortality rate between metropolitan areas, and the span that resulted in the strongest evidence (highest *P* value) to suggest no residual spatial structure. The risk estimates and SEs (and thus the confidence intervals) were estimated using generalized additive modeling[27] with S-Plus statistical software,[28] which provides unbiased effect estimates, but may underestimate SEs if there is significant spatial autocorrelation and significant correlations between air pollution and the smoothed surface of mortality. Therefore, evidence of spatial autocorrelation was carefully evaluated and tested using the Bartlett test.[29] The correlations of residual mortality with distance between metropolitan areas were graphically examined.

Analyses were also conducted of effect modification by age, sex, smoking status, occupational exposure, and education. Finally, models were fit using a variety of alternative pollution indices, including gaseous pollutants. Specifically, models were estimated separately for each of the pollution variables listed in Table 1, while also including all of the other risk factor variables.

RESULTS

Fine particulate air pollution generally declined in the United States during the follow-up period of this study. Figure 1 plots mean $PM_{2.5}$ concentrations for 1999-2000 over mean $PM_{2.5}$ concentrations for 1979-

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1983 for the 51 cities in which paired data were available. The concentrations of $PM_{2.5}$ were lower in 1999-2000 than in 1979-1983 for most cities, with the largest reduction observed in the cities with the highest concentrations of pollution during 1979-1983. Mean $PM_{2.5}$ levels in the 2 periods were highly correlated (r = 0.78). The rank ordering of cities by relative pollution levels remained nearly the same. Therefore, the relative levels of fine particle concentrations were similar whether based on measurements at the beginning of the study period, shortly following the study period, or an average of the 2.

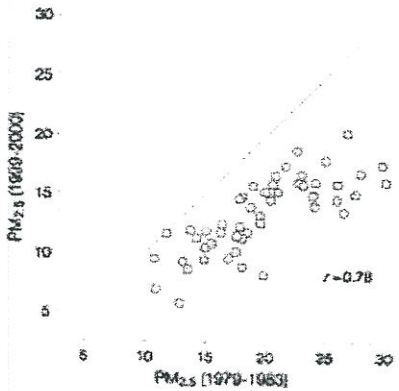

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Figure 1. Mean Fine Particles Measuring Less Than 2.5 μm in Diameter ($PM_{2.5}$)

Mean $PM_{2.5}$ concentrations in micrograms per meters cubed for 1999-2000 are plotted along with concentrations for 1979-1983 for the 51 metropolitan areas with paired pollution data. The dotted line is a reference 45°-equality line.

As reported in Table 2, all 3 indices of fine particulate air pollution were associated with all-cause, cardiopulmonary, and lung cancer mortality, but not mortality from all other causes combined. Figure 2 presents the nonparametric smoothed exposure response relationships between cause-specific mortality and $PM_{2.5}$ (average). The log RRs for all-cause, cardiopulmonary, and lung cancer mortality increased across the gradient of fine particulate matter. Goodness-of-fit tests indicated that the associations were not significantly different from linear associations (P>.20).

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Table 2. Adjusted Mortality Relative Risk (RR) Associated With a 10-μg/m^3 Change in Fine Particles Measuring Less Than 2.5 μm in Diameter

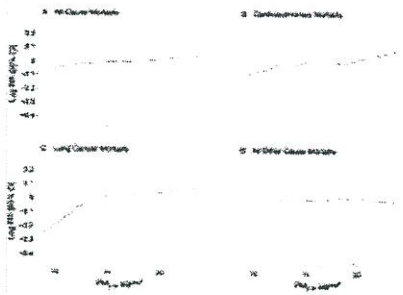

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Figure 2. Nonparametric Smoothed Exposure Response Relationship

Vertical lines along x-axes indicate rug or frequency plot of mean fine particulate pollution; $PM_{2.5}$, mean fine particles measuring less than 2.5 µm in diameter; RR, relative risk; and CI, confidence interval.

The fine particle mortality RR ratios from various alternative modeling approaches and assumptions are presented in Figure 3. After controlling for smoking, education, and marital status, the controlled forward stepwise inclusion of additional covariates had little influence on the estimated associations with fine particulate air pollution on cardiopulmonary and lung cancer mortality. As expected, cigarette smoking was highly significantly associated with elevated risk of all-cause, cardiopulmonary, and lung cancer mortality ($P<.001$). Estimated RRs for an average current smoker (men and women combined, 22 cigarettes/day for 33.5 years, with initiation before age 18 years) were equal to 2.58, 2.89, and 14.80 for all-cause, cardiopulmonary, and lung cancer mortality, respectively. Statistically significant, but substantially smaller and less robust associations, were also observed for education, marital status, BMI, alcohol consumption, occupational exposure, and diet variables. Although many of these covariates were also statistically associated with mortality, the risk estimates of pollution-related mortality were not highly sensitive to the inclusion of these additional covariates.

Figure 3. Mortality Relative Risk (RR) Ratio Associated With 10-µg/m^3 Differences of $PM_{2.5}$ Concentrations

Data presented are for 1979-1983 for the different causes of death, with various levels of controlling for individual risk factors, and using alternative modeling approaches. The 3 models with spatial smoothing allow for increasingly aggressive fitting of the spatial structure. Plus sign indicates model included previous variables (ie, smoking included stratification by age, sex, and race); $PM_{2.5}$, mean fine particles measuring less than 2.5 µm in diameter; and CI, confidence interval.

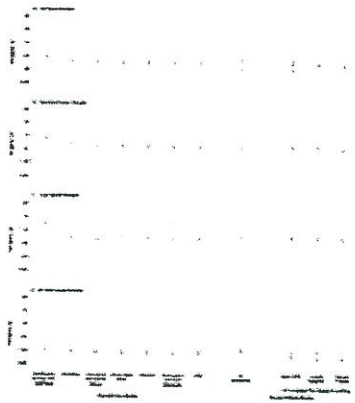

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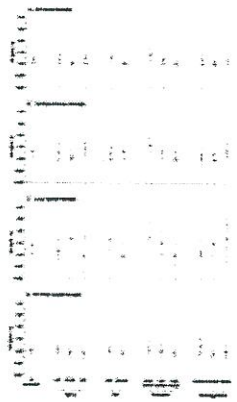
Figure 3 also demonstrates that the introduction of the random-effects component to the model resulted in larger SEs of the estimates and, therefore, somewhat wider 95% confidence intervals. There was no evidence of statistically significant spatial autocorrelation in the survival data based on the Bartlett test ($P>.20$) after controlling for fine particulate air pollution and the various individual risk factors. Furthermore, graphical examination of the correlations of the residual mortality with distance between metropolitan areas did not reveal significant spatial autocorrelation (results not shown). Nevertheless, the incorporation of spatial smoothing was included to further investigate the robustness of the estimated particulate pollution effect. Effect estimates were not highly sensitive to the incorporation of spatial smoothing to account for regional clustering or other spatial patterns in the data.

Figure 4 presents fine particle air pollution–related mortality RR ratios after stratifying by age, sex, education, and smoking status, and adjusting for all other risk factors. The differences across age and sex strata were not generally consistent or statistically significant. However, a consistent pattern emerged from this stratified analysis: the association with particulate pollution was stronger for both cardiopulmonary and lung cancer mortality for participants with less education. Also, for both cardiopulmonary and lung cancer mortality, the RR estimates were higher for nonsmokers.

Figure 4. Adjusted Mortality Relative Risk (RR) Ratio Associated With 10-μg/m^3 Differences of $PM_{2.5}$ Concentrations



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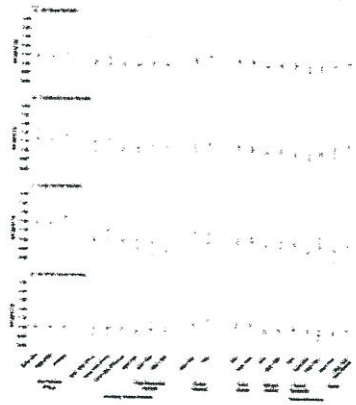
Data presented are for 1979-1983 for the different causes of death stratified by age, sex, education, and smoking status. $PM_{2.5}$ indicates mean fine particles measuring less than 2.5 μm in diameter; CI, confidence interval.

Figure 5 summarizes the associations between mortality risk and air pollutant concentrations listed in Table 1. Statistically significant and relatively consistent mortality associations existed for all measures of fine particulate exposure, including $PM_{2.5}$ and sulfate particles. Weaker less consistent mortality associations were observed with PM_{10} and PM_{15}. Measures of the coarse particle fraction ($PM_{15-2.5}$) and total suspended particles were not consistently associated with mortality. Of the gaseous pollutants, only sulfur dioxide was associated with elevated mortality risk. Interestingly, measures of $PM_{2.5}$ were associated with all-cause cardiopulmonary, and lung cancer mortality, but not with all other mortality. However, sulfur oxide pollution (as measured by sulfate particles and/or sulfur dioxide) was significantly associated with mortality from all other causes in addition to all-cause, cardiopulmonary, and lung cancer mortality.

Figure 5. Adjusted Mortality Relative Risk (RR) Ratio Evaluated at Subject-Weighted Mean Concentrations

$PM_{2.5}$ indicates particles measuring less than 2.5 μm in diameter; PM_{10}, particles measuring less than 10 μm in diameter; PM_{15}, particles measuring less than 15 μm in diameter; $PM_{15-2.5}$, particles measuring between 2.5 and 15 μm in diameter; and CI, confidence interval.



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This study demonstrated associations between ambient fine particulate air pollution and elevated risks of both cardiopulmonary and lung cancer mortality. Each 10-μg/m^3 elevation in long-term average $PM_{2.5}$ ambient concentrations was associated with approximately a 4%, 6%, and 8% increased risk of all-cause, cardiopulmonary, and lung cancer mortality, respectively, although the magnitude of the effect somewhat depended on the time frame of pollution monitoring. In addition, this analysis addresses many of the important questions concerning the earlier, more limited analysis of the large CPS-II cohort, including the following issues.

First, does the apparent association between pollution and mortality persist with longer follow-up and as the cohort ages and dies? The present analysis more than doubled the follow-up time to more than 16 years, resulting in approximately triple the number of deaths, yet the associations between pollution and mortality persisted.

Second, can the association between fine particulate air pollution and increased cardiopulmonary and lung cancer mortality be due to inadequate control of important individual risk factors? After aggressively controlling for smoking, the estimated fine particulate pollution effect on mortality was remarkably robust. When the analysis was stratified by smoking status, the estimated pollution effect on both cardiopulmonary and lung cancer mortality was strongest for never smokers vs former or current smokers. This analysis also controlled for education, marital status, BMI, and alcohol consumption. This analysis used improved variables to control for occupational exposures and incorporated diet variables that accounted for total fat consumption, as well as for

consumption of vegetables, citrus, and high-fiber grains. The mortality associations with fine particulate air pollution were largely unaffected by the inclusion of these individual risk factors in the models. The data on smoking and other individual risk factors, however, were obtained directly by questionnaire at time of enrollment and do not reflect changes that may have occurred following enrollment. The lack of risk factor follow-up data results in some misclassification of exposure, reduces the precision of control for risk factors, and constrains our ability to differentiate time dependency.

Third, are the associations between fine particulate air pollution and mortality due to regional or other spatial differences that are not adequately controlled for in the analysis? If there are unmeasured or inadequately modeled risk factors that are different across locations, then spatial clustering will occur. If this clustering is independent or random across metropolitan areas, then the spatial clustering can be modeled by adding a random-effects component to the Cox proportional hazards model as was done in our analysis. The clustering may not be independent or random across metropolitan areas due to inadequately measured or modeled risk factors (either individual or ecological). If these inadequately measured or modeled risk factors are also spatially correlated with air pollution, then biased pollution effects estimates may occur due to confounding. However, in this analysis, significant spatial autocorrelation was not observed after controlling for fine particulate air pollution and the various individual risk factors. Furthermore, to minimize any potential confounding bias, sensitivity analyses, which directly modeled spatial trends using nonparametric smoothing techniques, were conducted. A contribution of this analysis is that it included the incorporation of both random effects and nonparametric spatial smoothing components to the Cox proportional hazards model. Even after accounting for random effects across metropolitan areas and aggressively modeling a spatial structure that accounts for regional differences, the association between fine particulate air pollution and cardiopulmonary and lung cancer mortality persists.

Fourth, is mortality associated primarily with fine particulate air pollution or is mortality also associated with other measures of particulate air pollution, such as PM_{10}, total suspended particles, or with various gaseous pollutants? Elevated mortality risks were associated primarily with measures of fine particulate and sulfur oxide pollution. Coarse particles and gaseous pollutants, except for sulfur dioxide, were generally not significantly associated with elevated mortality risk.

Fifth, what is the shape of the concentration-response function? Within the range of pollution observed in this analysis, the concentration-response function appears to be monotonic and nearly linear. However, this does not preclude a leveling off (or even steepening) at much higher levels of air pollution.

Sixth, how large is the estimated mortality effect of exposure to fine particulate air pollution relative to other risk factors? A detailed description and interpretation of the many individual risk factors that are controlled for in the analysis goes well beyond the scope of this report. However, the mortality risk associated with cigarette smoking has been well documented using the CPS-II cohort.[16] The risk imposed by exposure to fine particulate air pollution is obviously much smaller than the risk of cigarette smoking. Another risk factor that has been well documented using the CPS-II cohort data is body mass as measured by BMI.[30] The Word Health Organization has categorized BMI values between 18.5-24.9 kg/m^2 as normal; 25-29.9 kg/m^2, grade 1 overweight; 30-39.9 kg/m^2, grade 2 overweight; and 40 kg/m^2 or higher, grade 3 overweight.[31] In the present analysis, BMI

values and BMI values squared were included in the proportional hazards models. Consistent with previous ACS analysis,[30] BMI was significantly associated with mortality, optimal BMI was between approximately 23.5 and 24.9 kg/m^2, and the RR of mortality for different BMI values relative to the optimal were dependent on sex and smoking status. For example, the RRs associated with BMI values between 30.0 and 31.9 kg/m^2(vs optimal) would be up to approximately 1.33 for never smokers. Based on these calculations, mortality risks associated with fine particulate air pollution at levels found in more polluted US metropolitan areas are less than those associated with substantial obesity (grade 3 overweight), but comparable with the estimated effect of being moderately overweight (grade 1 to 2).

In conclusion, the findings of this study provide the strongest evidence to date that long-term exposure to fine particulate air pollution common to many metropolitan areas is an important risk factor for cardiopulmonary mortality. In addition, the large cohort and extended follow-up have provided an unprecedented opportunity to evaluate associations between air pollution and lung cancer mortality. Elevated fine particulate air pollution exposures were associated with significant increases in lung cancer mortality. Although potential effects of other unaccounted for factors cannot be excluded with certainty, the associations between fine particulate air pollution and lung cancer mortality, as well as cardiopulmonary mortality, are observed even after controlling for cigarette smoking, BMI, diet, occupational exposure, other individual risk factors, and after controlling for regional and other spatial differences.

AUTHOR INFORMATION

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Analysis and interpretation of data: Pope, Burnett, Krewski, Thurston.

Drafting of the manuscript: Pope, Burnett, Ito, Thurston.

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Obtained funding: Pope, Thun, Thurston.

Administrative, technical, or material support: Pope, Calle, Krewski, Ito, Thurston.

Study supervision: Pope, Krewski.

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REFERENCES

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1. Firket J. The cause of the symptoms found in the Meuse Valley during the fog of December, 1930. *Bull Acad R Med Belgium.* 1931;11:683-741.

2. Ciocco A, Thompson DJ. A follow-up of Donora ten years after: methodology and findings. *Am J Public Health.* 1961;51:155-164.

3. Logan WPD, Glasg MD. Mortality in London fog incident, 1952. *Lancet.* 1953;1:336-338.

4. Pope III CA, Dockery DW. Epidemiology of particle effects. In: Holgate ST, Koren H, Maynard R, Samet J, eds. *Air Pollution and Health.* London, England: Academic Press; 1999:673-705.

5. Kaiser J. Showdown over clean air science. *Science.* 1997;277:466-469. FULL TEXT

6. World Health Organization-European Region. *Update and Revision of the Air Quality Guidelines for Europe.* Copenhagen, Denmark: World Health Organization-European Region; 1995. Document EUR/ICP/EHAZ 94 05/PB01.

7. CEPA/FPAC Working Group on Air Quality Objectives and Guidelines. *National Ambient Air Quality Objectives for Particulate Matter.* Ottawa, Ontario: Public Works and Government Services; 1998. Category No. H46-2/98-220.

8. Committee of the Environmental and Occupational Health Assembly of the American Thoracic Society. Health effects of outdoor air pollution. *Am J Respir Crit Care Med.* 1996;153:3-50. ABSTRACT

9. Committee on the Medical Effects of Air Pollution. *Non-Biological Particles and Health.* London, England: United Kingdom Dept of Health; 1995.

10. Environmental Protection Agency. *Air Quality Criteria for Particulate Matter.* Washington, DC: Environmental Protection Agency; 1996. Document EPA/600/P-95/001cf.

11. Samet JM, Dominici F, Curriero FC, Coursac I, Zeger SL. Fine particulate air pollution and mortality in 20 US cities. *N Engl J Med.* 2000;343:1742-1749. ABSTRACT/FULL TEXT

12. National Research Council. *Research Priorities for Airborne Particulate Matter, I: Immediate Priorities and a Long-Range Research Portfolio.* Washington, DC: National Academy Press; 1998.

13. National Research Council. *Research Priorities for Airborne Particulate Matter, III: Early Research Progress.* Washington, DC: National Academy Press; 2001.

14. *Whitman v American Trucking Associations Inc*, 532 US 457 (2001).

15. Dockery DW, Pope III CA, Xu X, et al. An association between air pollution and mortality in six US cities. *N Engl J Med.* 1993;329:1753-1759. ABSTRACT/FULL TEXT

16. Pope III CA, Thun MJ, Namboodiri MM, et al. Particulate air pollution as a predictor of mortality in a prospective study of US adults. *Am J Respir Crit Care Med.* 1995;151:669-674. ABSTRACT

17. Krewski D, Burnett RT, Goldberg MS, et al. *Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality: Special Report.* Cambridge, Mass: Health Effects Institute; 2000.

18. Chao A, Thun MJ, Jacobs E, Henley SJ, Rodriguez C, Calle EE. Cigarette smoking and colorectal cancer mortality in the Cancer Prevention Study II. *J Natl Cancer Inst.* 2000;92:1888-1896. ABSTRACT/FULL TEXT

19. Calle EE, Terrell DD. Utility of the National Death Index for ascertainment of mortality among Cancer Prevention Study II participants. *Am J Epidemiol.* 1993;137:235-241. ABSTRACT

20. US Postal Service. *1989 National Five Digit Zip Code and Post Office Directory.* Washington, DC: National Information Data Center; 1989.

21. Fleming TR, Harrington DP. *Counting Processes and Survival Analysis.* New York, NY: John Wiley & Sons; 1991.

22. Burnett R, Ma R, Jerrett M, et al. The spatial association between community air pollution and mortality: a new method of analyzing correlated geographic cohort data. *Environ Health Perspect.* 2001;109(suppl 3):375-380.

23. Easton DF, Peto J, Babiker GAG. Floating absolute risk: an alternative to relative risk in survival and case-control analysis avoiding an arbitrary reference group. *Stat Med.* 1991;10:1025-1035. ISI | MEDLINE

24. Burnett RT, Ross WH, Krewski D. Non-linear mixed regression models. *Environmetrics.* 1995;6:85-99. ISI

25. Siemiatycki J, Nadon L, Lakhani R, Beegin D, Geerin M. Exposure assessment. In: Siemiatycki J, ed. *Risk Factors for Cancer in the Workplace.* Baton Rouge, La: CRC Press; 1991:45-114.

26. Cleveland WS, Devlin SJ. Robust locally weighted regression and smoothing scatterplots. *J Am Stat Assoc.* 1988;74:829-836.

27. Hastie T, Tibshirani R. *Generalized Additive Models.* London, England: Chapman & Hall; 1990.

28. *S-Plus 2000 Programmer's Guide.* Seattle, Wash: Math Soft; 2000.

29. Priestly MB. *Spectral Analysis and Time Series.* London, England: Academic Press; 1981.

30. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of US adults. *N Engl J Med.* 1999;341:1097-1105. ABSTRACT/FULL TEXT

31. Physical status: the use and interpretation of anthropometry: report of a WHO expert committee. *World Health Organ Tech Rep Ser.* 1995;854:1-452. ISI | MEDLINE

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Committee on Environmental Health
Pediatrics 2004;114:1699-1707.
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Occup Environ Med 2004;61:757-763.
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FULL TEXT

Traffic Air Pollution and Mortality Rate Advancement Periods
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Circulation 2004;109:2655-2671.
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Somers et al.
Science 2004;304:1008-1010.
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Hoskins
Indoor and Built Environment 2003;12:69-72.
ABSTRACT

Cost Analysis of the Built Environment: The Case of Bike and Pedestrian Trials in Lincoln, Neb
Wang et al.
Am J Public Health 2004;94:549-553.
ABSTRACT | FULL TEXT

Association of Higher Levels of Ambient Criteria Pollutants with Impaired Cardiac Autonomic Control: A Population-based Study
Liao et al.
Am. J. Epidemiol. 2004;159:768-777.
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Effect of Ambient Air Pollution on Pulmonary Exacerbations and Lung Function in Cystic Fibrosis
Goss et al.
Am J Respir Crit Care Med 2004;169:816-821.
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Effects of sham air and cigarette smoke on A549 lung cells: implications for iron-mediated oxidative damage
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Ambient air pollution and health
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Br Med Bull 2003;68:143-156.
ABSTRACT | FULL TEXT

Predicted health impacts of urban air quality management
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ABSTRACT | FULL TEXT

Cardiovascular pathophysiology of environmental pollutants
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Am. J. Physiol. 2004;286:H479-485.
FULL TEXT

Cardiovascular Mortality and Long-Term Exposure to Particulate Air Pollution: Epidemiological Evidence of General Pathophysiological Pathways of Disease
Pope et al.
Circulation 2004;109:71-77.
ABSTRACT | FULL TEXT

Pulmonary Inflammation and Thrombogenicity Caused by Diesel Particles in Hamsters: Role of Histamine
Nemmar et al.
Am J Respir Crit Care Med 2003;168:1366-1372.
ABSTRACT | FULL TEXT

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Thorax 2003;58:1071-1076.
ABSTRACT | FULL TEXT

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Thorax 2003;58:1010-1012.
FULL TEXT

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Heart 2003;89:1383-1388.
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Risom et al.
Carcinogenesis 2003;24:1847-1852.
ABSTRACT | FULL TEXT

Changes in lung permeability and lung mechanics accompany homeostatic instability in senescent mice
Tankersley et al.
J. Appl. Physiol. 2003;95:1681-1687.

ABSTRACT | FULL TEXT

Relation between income, air pollution and mortality: a cohort study
Finkelstein et al.
Can Med Assoc J 2003;169:397-402.
ABSTRACT | FULL TEXT

Air Pollution Particles Produce Airway Wall Remodeling in Rat Tracheal Explants
Dai et al.
Am J Respir Cell Mol Biol 2003;29:352-358.
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Burstyn et al.
Am. J. Epidemiol. 2003;158:468-478.
ABSTRACT | FULL TEXT

Particulate Matter Induces Alveolar Epithelial Cell DNA Damage and Apoptosis: Role of Free Radicals and the Mitochondria
Upadhyay et al.
Am J Respir Cell Mol Biol 2003;29:180-187.
ABSTRACT | FULL TEXT

Temporal variation of hydroxyl radical generation and 8-hydroxy-2'-deoxyguanosine formation by coarse and fine particulate matter
Shi et al.
Occup Environ Med 2003;60:315-321.
ABSTRACT | FULL TEXT

The biological effects of coarse and fine particulate matter
Donaldson
Occup Environ Med 2003;60:313-314.
FULL TEXT

Personal Exposure to PM2.5 and Biomarkers of DNA Damage
Sorensen et al.
Cancer Epidemiol Biomarkers Prev 2003;12:191-196.
ABSTRACT | FULL TEXT

Measuring the accumulated hazards of smoking: global and regional estimates for 2000
Ezzati and Lopez
Tob Control 2003;12:79-85.
ABSTRACT | FULL TEXT

Diesel Exhaust Particles in Lung Acutely Enhance Experimental Peripheral Thrombosis
Nemmar et al.
Circulation 2003;107:1202-1208.
ABSTRACT | FULL TEXT

Primary Prevention Protects Public Health
TOMATIS
Annals NYAS Online 2002;982:190-197.
ABSTRACT | FULL TEXT

Global Climate Change and Air Pollution: Common Origins With Common Solutions
Bransford and Lai
JAMA 2002;287:2285-2285.
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OTHER ARTICLES NOTED (Nov 01 to 18 Oct 02)
Evid Based Nurs 2003;6:e1-1.
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Finkelstein et al.
JAMA 2002;288:830-830.
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Quantification of health effects of exposure to air pollution
Krzyzanowski et al.
Occup Environ Med 2002;59:791-793.
FULL TEXT

Mutagenicity and in Vivo Toxicity of Combined Particulate and Semivolatile Organic Fractions of Gasoline and Diesel Engine Emissions
Seagrave et al.
Toxicol. Sci. 2002;70:212-226.
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How important is personal exposure assessment in the epidemiology of air pollutants?
Cherrie
Occup Environ Med 2002;59:653-654.
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Circulation 2002;106:890-892.
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On the Use of Generalized Additive Models in Time-Series Studies of Air Pollution and Health
Dominici et al.
Am. J. Epidemiol. 2002;156:193-203.
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